EJCM
ejcvsmed.com

E Journal of Cardiovascular Medicine

Volume 7 | Issue 1

March 2019

www.ejcm.com & www.ejcvsmed.com

HEART AND HEALTH FOUNDATION OF TURKEY

galenos yayınevi

Editor-in-Chief

Asistant Editors

www.ejcvsmed.com

galenos yayınevi

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1
34093 İstanbul, Turkey
Phone: +90 (212) 621 99 25 Fax: +90 (212) 621 99 27
E-mail: info@galenos.com.tr/yayin@galenos.com.tr
Web: www.galenos.com.tr | Publisher Certificate Number: 14521

Online Publishing Date: March 2019
E-ISSN: 2147-1924
International scientific journal published quarterly.

International Scientific Advisory Board

Owner

©TÜSAV Heart and Health Foundation of Turkey

Administration Office

Şair Eşref Bulvarı, 1402 Sk. No: 2/2 Özbaş Apt.
Alsancak / Izmir / Turkey

Tel.: + 90 232 464 19 63 / **Fax:** +90 232 464 24 70

e-mail: info@oztekinoto.com | info@tksv.com

Dr. Silvio Nocco

Sirai Hospital, Department of Cardiology, Carbonia / Italy

Assoc. Prof. Zeynep Tuğba Özdemir

Bozok University School of Medicine, Internal Medicine, Yozgat / Turkey

Dr. Tanıl Özer

Kartal Koşuyolu Yüksek İhtisas Research and Education Hospital, Istanbul / Turkey

Prof. Murat Özeren

Mersin University Medical School, Cardiovascular Surgery, Mersin / Turkey

Assoc. Prof. Emre Özker

Başkent University School of Medicine, Department of Cardiovascular Surgery, Ankara / Turkey

Dr. Abdullah Özyurt

Mersin Maternity and Children Diseases Hospital, Pediatric Cardiology, Mersin / Turkey

Dr. Recep Oktay Peker

Hacettepe University, Department of Cardiovascular Surgery, Ankara / Turkey

Dr. Hikmet Sahratov

Gülhane Education and Research Hospital, Department of Cardiovascular Surgery, Ankara / Turkey

Dr. Gonzalo Luis Alonso Salinas

Marcelo Sanmartín of Hospital Universitario Ramón y Cajal, Madrid / Spain

Dr. Stefano Salizzoni

Città della Salute e della Scienza, Cardiac Surgery, Cardiac Surgery, Turin / Italy

Dr. Gökhan Sargın

Adnan Menderes University Medical School, Internal Medicine, Aydın / Turkey

Dr. Mustafa Seren

Ankara 29 Mayıs State Hospital and Cardiovascular Surgery, Ankara / Turkey

Prof. Erdem Silistreli

Dokuz Eylül University, Department of Cardiovascular Surgery, İzmir / Turkey

Assoc. Prof. Ömer Tanyeli

Necmettin Erbakan University, Meram Midical Faculty Hospital, Cardiovascular Surgery, Konya / Turkey

Dr. İlker Tekin

Antalya Medicalpark Hospital, Cardiovascular Surgery, Antalya / Turkey

Assist. Prof. Dinçer Uysal

Isparta Süleyman Demirel University, Department of Cardiovascular Surgery, Isparta / Turkey

Dr. Olivier Villemain

IM3C Necker-Enfants Malades, AP-HP, Université Paris Descartes, Pediatric Cardiology, Radiology, Paris / France

Dr. Mustafa Esat Yamaç

Ahi Evren University of Health Sciences, Thoracic and Cardiovascular Surgery, Trabzon / Turkey

Assoc. Prof. Ali Ümit Yener

Canakkale Onsekiz Mart University Medical Faculty, Department of Cardiovascular Surgery, Çanakkale / Turkey

Dr. Dilek Yeşilbursa

Uludağ University, Medical Faculty, Department of Cardiology / Bursa / Turkey

Dr. Mustafa Yılmaz

Sami Ulus Training and Research Hospital, Pediatric Cardiology / Ankara / Turkey

Volume 7 | Issue 1 | March 2019

Review Article

Research Articles

Case Reports

Letter to the Editor

E Journal of Cardiovascular Medicine
ejcvsmed.org
Review Article
1
EJCM 2019;7(1):1-8
DOI: 10.32596/ejcm.galenos.2019.00012

Carotid Endarterectomy in Awake Patient: Review Article

İbrahim Erdinç

University of Health Sciences, İzmir Bozyaka Training and Research Hospital, Clinic of Cardiovascular Surgery, İzmir, Turkey

Abstract

Cardiac mortality and morbidity in patients undergoing carotid surgery is between 0.7% and 7.1%. Although surgical techniques used in carotid surgery varies, there are differences in anesthesia techniques and the results are different. The advantages and disadvantages of anesthesia techniques are discussed in several studies and various results have been obtained. These different results involve the acquisition or loss of anesthesia technique, even if the patient group is the same. Carotid surgery under loco/regional anaesthesia may be thought easy. Although the complex structure of the head and neck region takes difficulty of during surgery, direct cerebral monitorization in the awake patient increases the success rate of the surgery. In this review we will explain the carotid endarterectomy management in the awake patient.

Keywords: Awake, carotid stenozis, locoregional cervical blocage, carotid endarterectomy

Introduction

Carotid endarterectomy (CEA) is a surgical procedure to remove the endothelium and atherosclerotic plaque from inside the carotid artery wall. CEA may be performed under general (GA) or regional/local (LA) anaesthesiadepending on the preferences of the individual surgeon, anaesthetist and patient[1]. Stroke is the third leading cause of death and probably the most important cause of long-term disability[1]. CEA has become recognized as reliable in relieving symptoms of transient ischemic attacks and, more importantly, in the prevention of strokes due to arteriosclerotic disease at the carotid bifurcation[2].

Eastcott performed carotid reconstruction for symptomatic internal carotid artery stenosis in 1954 under general anaesthesia for extracranial carotid obstruction[3].

Carotid endarterectomy is a surgical procedure to remove the endothelium and atherosclerotic plaque from inside the carotid artery wall. Carotid endarterectomy

Address for Correspondence: İbrahim Erdinç, University of Health Sciences, İzmir Bozyaka Training and Research Hospital, Clinic of Cardiovascular Surgery, İzmir, Turkey
Phone: +90 532 426 10 55 **e-mail:** patentheart@yahoo.com
Received: 27.02.2019 **Accepted**: 06.03.2019

Cite this article as: Erdinç İ. Carotid Endarterectomy in Awake Patient: Review Article. EJCM 2019;7(1):1-8.
DOI: 10.32596/ejcm.galenos.2019.00012

(CEA) may be performed under general (GA) or regional/ local (LA) anaesthesiadepending on the preferences of the individual surgeon, anaesthetist and patient[4]. Tangkanakul et al. studied regional or local anaesthesia, which was preferred by most of the pioneers of CEA. However, there was concern about intraoperative cerebral ischaemia. After Wells published his series in 1963 suggesting that general anaesthesia may confer a cerebral protective effect, this technique was widely adopted[13]. Interest in loco-regional anaesthesia was subsequently revived by surgeons who believed that awake testing was the only reliable method of monitoring cerebral oxygenation. Nevertheless most surgeons continued to operate under general anaesthesia. Ultimately a generation of vascular surgeons and anaesthetists were trained to perform CEA under general anaesthesia utilising a wide variety of imperfect monitoring techniques.

Surgical Technique

CEA can be were performed either with deep or superficial regional anesthesia. Superficial cervical block was performed with the injection of 10 cc bupivacaine 0.05%, 6 cc lidocaine 2% and 4 cc saline combination along the lateral border of the sternocleidomastoid muscle subcutaneously. Deep cervical plexus block was performed at C2, C3, and C4 level of the transverse processes of cervical vertebrae A combination of lidocaine hydrochloride and bupivacaine hydrochloride was injected after negative aspiration result for blood. A total amount of bupivacaine hydrochloride 2-3 mg/kg was allowed. Additional prilocaine hydrochloride was used subcutaneously at the incision line as infiltration anesthesia. Additional doses of prilocaine hydrochloride was injected intraoperatively if the patient complained of pain during the procedure. The allowed total dose of prilocaine was 5 mg/kg. Intraoperative remifentanil (0.025-0.05 mg/kg/min) maintained an adequate level of comfort, responsiveness, and cooperation. Continuous infusion of nitroglycerin was used for blood pressure control. Additional diltiazem or metoprolol was administered if needed. After de-clamping occasionally midazolam was given. Systemic heparin (100 IU/kg) was injected before clamping and was not antagonized after the procedure. A shunt was selectively used in case of neurologic deterioration at cross-clamping test at duration of 2-3 minutes.[16,17,20]

A standard incision parallel to the sternocleidomastoid muscle was performed and common carotid artery, internal carotid artery, and external carotid artery were prepared and dissected. After administrationof 5000 IU heparin intravenously, the arteries were clamped. The consciousness and the neurologic status of the patient were evaluated with patient's response to verbal stimuli and ability to move contralateral side hand and foot for at least 2-3 minutes prior to arteriotomy. In case of neurologic disturbance, endarterectomy was performed with insertion of a shunt. The CEA with or without patchplasty was performed as usual fashion. The symptomatic otherwise more stenotic side was prioritized followed by the surgery of the contralateral side in cases with bilateral carotid disease. The optimal anesthetic tecgnique for during CEA is controversial. Advocates of regional anesthesia suggest that it may reduce the incidence of perioperative complications in addition to decreasing operative time and hospital costs. The techniques of local and regional (cervical plexus block) anesthesia for carotid surgery have been described and used since before 1962[5]. CEA surgery is commonly performed under cervical plexus blocks[6,7]. This is presumed to offer advantages over general anaesthesia in terms of monitoring neurological function during cross-clamping of the carotid artery since, in conscious patients, speech, cerebration, and motor power provide early measures of inadequate cerebral perfusion[8].

Some studies also claim lower shunting requirements, lower cardiovascular morbidity, and shorter hospital stay at awake patients under CEA[9]. The techniques of local and cervical-block anesthesia for carotid surgery have been described and used since before 1962[10]. During the infancy of the procedure, regional anesthesia with cervical blockage in right atrium (RA) was felt to be

essential to the safety of the operation by preventing cerebral depression, reducing blood pressure, and allowing close observation of any neurologic changes during the operation[1,2]. There is no consensus as to which is the superior technique, but evidence from several non-randomised series suggests that LA offers considerable benefits, including a reduction in shunt placement, a reduction in mortality and major morbidity and decreased length of hospital stay[11]. Tangkanakul et al. Awake testing Hesitancy in response Gold standard Local anaesthesia Loss of consciousness Requires good communication with patient[4]. Although the studies generally reported that the patients having LA and GA were compatible in terms of age, sex and vascular risk factors, this certainly does not imply that they were similar for all important prognostic factors.

In some patients the operation may be technically more difficult under LA, e.g. in those with short, fat necks. Some patients, perhaps 10%, 34 will also refuse to have the operation under LA ~ind some surgeons may refuse to perform the operation under LA. Pandit et al. reported that, in modern anaesthetic practice, cervical plexus blockade can be elegantly performed under ultrasound guidance with a high success rate and a low risk of procedural complications, even in patients taking dual antiplatelet therapy and in those with prior cervical surgery[12].

Advantages of GA are:

• Control of ventilation (tight control of arterial carbon dioxide concentration)[13-17]

• Cerebral protection afforded by volatile anaethesia (especially during the cross-clamp)[13,18,15,19-21]

• Airway security (anaesthetist preference)[13,22,15,19,17]

• Excellent and comfortable operation conditions (especially in patients with high carotid bifurcation)[14,17,19-21]

• Prevent myocardial ischemia[19]

• Less stressful than a regional procedure[14,20]

• Prevent patients from coughing and straining[19]

• Possibility of inducing hypothermia if required[15]

Disadvantages of GA are:

• GA necessitates shunt insertion more commonly than RA techniques[14,15,23,27]

• Requires brain monitoring (stump pressure, somatosensory evoked potential, transcranial Doppler, electroencephalogram and near-infrared spectroscopy, juguler venous oxygen,cerebral oximetry)[3,7,9,24,30]. These methods shows poor sensitivity and specificity according to awake patient, in terms of requirement for shunt placement[15,24]

• Anaesthetic-induced circulatuar depression is associated with labile blood pressure[3] and necessitates greater vasopressor support (To ensure adequate cerebral perfusion pressure during carotid cross-clemping)[14,15,25,26,]

• Higher incidence in postoperative neurocognitive dysfunction[15,17]

Advantages of regional anesthesia are:

• Awake patient is the gold standart cerebral function monitoring[14,15,17,20,21]

• Reduce cardiac and respiratory related morbidity[15,16,18,20]

• Lower shunt insertion rate[14,15,17,19,21,24]

• Shorten hospital stay[14,15,17,19,21,24]

• Lower cost[14,15,18,21]

• Improves outcomes after surgery (better postoperative analgesia, reduce blood loss, lower risk of tromboembolic events)[15,18,20,22]

• Safer[14]

• Safe method to identify the patients at risk for cross-clamp intolerance [1,3,12]

• Hemodynamic stability[14,17,18,21,22,24,27]

• Preserved cerebral autoregulation[14,16,18,24,25]

• Reduce vasopressor requirement[25]

• Reduces operative time[24]

Disadvantages of regional anesthesia are:

• Needs patient collaboration[14,16,23,28]

• Procedural complications (diaphragmatic and vocal cord paralysis, neural injuries, epidural, subaracnoid or intravascular injection of local anaesthetics)[15]

• Urgent conversion of regional anesthesia into general anesthesia[15,16,26]

• Anxiety during the operation[14,16]

Regarding complications, superficial cardiopulmonary bypass (CPB) is associated with the common adverse effects of any nerve block such as inadvertent intravascular injection of local anesthetic and local anesthetic toxicity. In addition to these effects, deep CPB increases the occurrence of complications arising from the placement of the block, including accidental intravascular injection into the vertebral artery, subdural injection resulting in subarachnoid block, large neck hematoma, bilateral recurrent laryngeal nerve palsy, and phrenic nerve palsy[28-30]. All trials showed that blood pressure tended to increase during clamping of the carotid artery in the LA group, and in two studies there were significantly more patients with significant hypertension in the LA group during surgery (Forssell 0% vs 36%; Pluskwa 20% vs 80%). In general, hypertension seemed more common during surgery in the GA group, whilst hypotension postoperatively was more common in the LA group. There were also significantly lower odds of myocardial infarction within 30 days of surgery in patients under LA. Only a few studies assessed local haemorrhage and cranial nerve palsies. There were no significant differences between the two groups for these outcomes, the confidence intervals were wide. Only five studies reported pulmonary complications. The definition of pulmonary complication varied between different studies and included pneumonia, pulmonary emboli and prolonged intubation. These complications were very rare but there were significantly fewer pulmonary complications in the LA group[32,33]. Shunting during CEA remains controversial and, while there is no conclusive data to support or refuse the use of routine or selective shunting in carotid surgery, there is consensus that either policy is preferable to a policy of routine non-shunting[8,9]. Shunts can give rise to complications and in our opinion the finite risk of stroke associated with their use is reason enough to avoid them[10,11]. Techniques including stump pressure measurement, electroencephalography, regional cerebral blood flow measurements, near infrared spectroscopy and transcranial doppler have all been used to monitor cerebral function during GA for CEA, but none have been shown to be absolutely reliable in predicting the outcome of cross clamping. This is largely because individual patients vary in their susceptibility to reduced cerebral blood flow. The principle advantage of LA for CEA is the ability to monitor patients with direct neurological assessment and selectively shunt if they develop neurological signs[12,14]. Indeed for those surgeons who adopt a policy of selective shunting, CEA under LA is the only method capable of predicting accurately which patients need a shunt. As expected, many fewer shunts were inserted in those who had the operation under LA compared to GA (10.8% vs 44.3%, OR 0.12, 95% CI 0.10-0.14). However, there was significant heterogenity in the overall result[31-38,58].

Median hospital length of stay (LOS) for GA was significantly longer compared with RA (2.0 vs 1.2 days, $p<0.001$). Patients who received GA were also more likely to be admitted to the intensive care unit[39]. The cranial nerves (CN) can be injured during CEA by the surgical dissection, traction, electrocautery, clamp injury, or compression by a postoperative hematoma. The most commonly injured nerves are the recurrent or superior laryngeal branches of the vagus nerve (CN X-) glossopharyngeal nerve (CN IX). (Dysphagia, hoarseness, Ipsilateral vocal cord paralysis on laryngoscopy), the hypoglossal nerve (CN XI- Ipsilateral tongue deviation), the marginal mandibular branch of the facial nerve (CN VII- Ipsilateral facial droop, Inability to depress ipsilateral corner of lip), and the depending on the nerve that is injured, deficits vary from a minor nuisance to a severe disability that may require a feeding tube or tracheostomy, or both.

Health-related quality of life was affected in patients with Chronic Nerve Irritation (CNI) only with respect to eating and swallowing at the 2-week and 1-month

assessment, but this finding was no longer present at 1 year. On the basis of these findings, we conclude that CNI is not a trivial consequence of CEA but rarely results in significant long-term disability[40]. An interesting finding of this meta-analysis is that the incidence of hypoglossal nerve injury has significantly decreased from about 8% to 2% over the last 35 years, with a mean reduction rate of 0.18% per year. Similarly, the incidence of vagus nerve injury has decreased (8% in 1980 to <1% nowadays), with a mean reduction rate of 0.19% per year. Although the exact reason for this decreased incidence cannot be revealed by statistical means in this meta-analysis, it is probably due to increased awareness of this kind of injury and the preventive measures taken against them. The vagus nerve appears to be the most frequently injured cranial nerve after CEA, followed by the hypoglossal nerve. Most of these injuries are transient, recovering within 6-12 months, with the recovery rate being highest in the glossopharyngeal nerve and lowest in the vagus nerve[41]. Median overall costs for GA were significantly higher than median costs for RA [medians (with interquartile ranges), $10,140 ($7,158-$12,658) versus $7,122 ($5,072-$8,511), p<0.001][39]. A meta-analysis of 41 non-randomised studies (25,000 CEAs) reported that CEA under locoregional anaesthesia (LRA) was associated with a 40% RRR in 30-day death/stroke, compared with CEA under general anaesthesia (GA), as well as significant reductions in myocardial infarction (MI) and respiratory complications. Two hundred and sixty four, The General Anaesthesia Local Anaesthesia (GALA) trial (3526 patients), which is the largest RCT to date, reported no significant difference regarding perioperative death, stroke, or MI between GA (4.8%) and LRA (4.5%). Two hundred and sixty five, an updated Cochrane review, 266 which combined data from 14 RCTs (4596 patients), showed that CEA under LRA did not confer significant reductions in 30-day stroke (3.2%), compared with CEA under GA (3.5%) [42]. Surgical operative time was significantly less for LA procedures, which supports the results of series[43]. CEA under LA offers several advantages over GA. These include continuous accurate neurological monitoring, decreased shunting, less intraoperative hypotension, decreased operative time and shorter hospital stays with important implications for future resource management[44]. Anesthesia time, operative time, and frequency of shunt usage were significantly greater in the general anesthesia group (p<0.03)[45]. Hemodynamic instability during CEA is often a major concern in a patient population be set by symptomatic or occult coronary artery disease. Hypertension in particular has been implicated in perioperative neurologic complications[1,2] and may be associated with increased use of critical care facilities and longer hospital stays[3,4]. The potential advantages of regional anesthesia for CEA include more accurate neurologic monitoring with a decreased need for intraoperative shunting and a reduction in risk associated with general anesthesia (GA) in a high-risk population. Patients who undergo CEA with CB have significantly less perioperative hemodynamic instability, suffer fewer major cardiac complications, needs for ICU admission was less frequently, and experience shorter hospital stays than the patients who undergo CEA with GA. This may result in lower costs but certainly supports consideration of the preferential use of CB in patients with substantial cardiac risks who would tolerate large blood pressure and heart rate (HR) shifts poorly[46]. Employing LA rather than GA for CEA has been associated with a reduction in intraoperative shunting and perioperative stroke, and the duration of hospital stay. LA appears to offer clinical and possible cost advantages over GA (regional versus general anaesthesia for CEA: Impact of change in practiceIn a unit where CEA is preferentially performed under LA, anesthesia technique failed to significantly influence outcome. Local anaesthesia enables the surgeon to assess the level of cerebral perfusion with an awake patient, gives greater assurances of cerebral protection during arterial clamping and a provides for a more relaxed and cautious endarterectomy and repair[47]. Gurer et al. reported that LA was associated with a significantly lower operation time, shunt usage rate, length of hospital stay, and rates of permanent stroke. Restenos rates, neurological events,

and deaths were similar in the 2 groups at long-term follow-up[48]. However, the rate of shunt placement as well as operative time was lower in LA group than the general anesthesia group. Similarly, intensive care unit requirement, duration of hospital stay, and treatment costs were also lower in the local anesthesia group[49,50].

GALA trial was a multicenter (95 centers in 24 countries), randomized controlled study comparing LA and GA during surgery in 3526 patients who had either symptomatic or asymptomatic carotid stenosis. It showed no significant difference between the two study groups at 30-day follow-up with respect to death, stroke, stroke or death, myocardial infarction, and length of hospital stay[51]. CEA in awake patient allows close follow-up of neurological functions and decision regarding necessity of intraarterial shunt during surgery. Use of intraluminal shunt and general anesthesia are routinely recommended in most studies, but unpleasant complications during placement of shunt into the internal carotid artery are well known[52,53]. Anesthesia is the one of the most controversial issues of CEA. Detailed studies have reported cervical blockage has better results concerning perioperative stroke and cardiac events, such as arrhythmia and infarction[54]. The first Cochrane review on the subject was published in 1996 and was last updated in 2013. Neither the latest Cochrane review nor the GALA trial-the single largest trial available-have shown a statistically significant difference in outcomes between general and local anesthesia for CEA, in respect to 30-day incidence of stroke, MI, and mortality. These studies report a trend toward lower operative mortality with local anesthetic[51,55]. Recently, increased data in favor of the locomotive have emerged compared to general anesthesia. Hussain et al., who used the Michigan Surgical Quality Collaborative database, reported that general anesthesia for CEA was associated with more than twice mortality rate compared to regional anesthesia. Leichtle et al. reported that general anesthesia is an independent risk factor for postoperative MI, especially in patients with preoperative neurological symptoms[56,57].

Conclusion

The awake patient still has controversial parts of the carotid surgery. In many studies, as described and discussed herein, although awake patient during CEA have many advantages, in many clinics CEA is still have been performing under general anaesthesia. Perhaps the most important result of this report is, CEA being performed by local or regional techniques is that, the awake patient is the most important indicator for for direct cerebral monitoring. I performed CEA surgery in 800 patients under regional anesthesia in my institution. The patient's awake during surgery enables both the surgeon to communicate with the patient and facilitates the anesthesiologist to recognize possible complications (embolism, cross clemp intolarance). I believe that performing CEA surgery in the awake patient reduces postoperative hypotension, duration of ICU stay, postoperative complications (lung and heart) and perioperative shunt use.

Acknowledgements

I thank Fulya Yılmaz; University of Health Sciences, İzmir Bozyaka Training and Research Hospital, Clinic of Anaesthesiology and Reanimation, İzmir, Turkey, and Murat Uğurlucan, İstanbul University, Medical Faculty, Department of Cardiovascular Surgery, İstanbul for his comments on the manuscript.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Financial Disclosure: The author declared that this study received no financial support.

References

1. Bonita R. Epidemiology of stroke. Lancet 1992;339:342-4
2. Clauss RH, Sanoudas GM, Ray JF 3rd, Moallem S. Carotid endarterectomy for cerebrovascular ischemia. Surg Gynceol Obstet 1973;136:993-1000.

3. Eastcott HH, Pickering GW, Rob CG. Reconstruction of internal carotid artery in a patient with intermittent attacks ofhemiplegia. Lancet 1954;2:994-6.

4. Tangkanakul C, Counsell CE, Warlow CP. Local versus general anaesthesia in carotid endarterectomy: a systematic review of the evidence. Eur J Vasc Endovasc Surg 1997;13.491-9.

5. Spencer FC, Eısemann B. Technique of carotid endarterectomy. Surg Gynecol Obstet 1962;115:115-7.

6. Pandit JJ, Bree S, Dillon P, Elcock D, McLaren ID, Crider B. A comparison of superficial versus combined (superficial and deep) cervical plexus block for carotid endarterectomy: a prospective, randomized study, Anesth Analg 2000;91:781-6.

7. Pandit JJ, McLaren ID, Crider B. Efficacy and safety of the superficial cervical plexus block for carotid endarterectomy. Br J Anaesth 1999;83:970-2.

8. Andersen CA, Rich NM, Collins GJ Jr, McDonald PT. Carotid endarterectomy: regional versus general anesthesia. Am Surg 1980;46:323-7.

9. Benjamin ME, Silva MB Jr, Watt C, McCaffrey MT, Burford-Foggs A, Flinn WR. Awake patient monitoring to determine the need for shunting during carotidendarterectomy. Surgery 1993;114:673-9.

10. Spencer FC, Elsemann B. Technique of carotid endarterectomy. Surg Gynecol Obstet 1962;115:115-7.

11. Tangkanakul C, Counsell C, Warlow C. Local versus general anaesthesia for carotid endarterectomy. Cochrane Database Syst Rev 2000:CD000126.

12. Pandit JJ, Satya-Krishna R, Gration P. Superficial or deep cervical plexus block for carotid endarterectomy: a systematic review of complications. Br J Anaesth 2007;99:159-69.

13. Patelis N, Diakomi M, Maskanakis A, Maltezos K, Schizas D, Papaioannou M. General versus local anesthesia for carotid endarterectomy: Special considerations. Saudi J Anaesth 2018;12:612-7.

14. Kavaklı AS, Ayoğlu RU, Öztürk NK, et al. Simultaneous Bilateral Carotid Endarterectomy under Cervical Plexus Blockade. Turk J Anaesth Reanim 2015;43:367-70.

15. Zdrehuş C. Anaesthesia for carotid endarterectomy - general or loco-regional? Rom J Anaesth Intensive Care 2015;22:17-24.

16. Licker M. Regional or general anaesthesia for carotid Endarterectomy Does it matter? Eur J Anaesthesiol 2016;33:241-3.

17. Ciccozzi A, Angeletti C, Guetti C, et al. Regional anaesthesia techniques for carotid surgery: the state of art. J Ultrasound 2014;17:175-83.

18. Samanta S, Samanta S, Panda N, Haldar R. A unique anesthesia approach for carotid endarterectomy: Combination of general and regional anesthesia. Saudi J Anaesth 2014;8:290-3.

19. Casutt M, Breitenmoser I, Werner L, Seelos R, Konrad C. Ultrasound-guided carotid sheath block for carotid endarterectomy: a case series of the spread of injectate. Heart Lung Vessels 2015;7:168-76.

20. Leblanc I, Chterev V, Rekik M, Boura B, Costanzo A, Bourel P, et al. Safety and efficiency of ultrasound-guided intermediate cervical plexus block for carotid surgery. Anaesth Crit Care Pain Med 2016;35:109-14.

21. Rössel T, Kerstring S, Heller AR, Koch T. Combınation of high-resolution ultrasound-guided perivascular regional anesthesia of the internal carotid artery and intermediate cervical plexus block for carotid surgery. Ultrasound Med Biol 2013;39:981-6.

22. Hye RJ, Voeks JH, Malas MB, Tom ML, Longson S, Blackshear JL, et al. Anesthetic type and risk of myocardial infarction after carotid endarterectomy in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). J Vasc Surg 2016;64:3-8.

23. Lomivorotov VV, Shmyrev VA, Moroz GB. Volatile Anesthesia for Carotid Endarterectomy: Friend or Foe for the Brain? J Cardiothorac Vasc Anesth 2018;32:1709-10.

24. Lee J, Huh U, Song S, Chung SW, Sung SM, Cho HJ. Regional Anesthesia with Dexmedetomidine Infusion: A Feasible Method for the Awake Test during Carotid Endarterectomy. Ann Vasc Dis 2016;9:295-9.

25. Tsujikawa S, Ikeshita K. Low-dose dexmedetomidine provides hemodynamics stabilization during emergence and recovery from general anesthesia in patients undergoing carotid endarterectomy: a randomized double-blind, placebo-controlled trial. J Anesth 2019.

26. Sideso E, Walton J, Handa A. General or Local Anesthesia for Carotid Endarterectomy--The ‘‘Real-World’’ Experience. Angiology 2011;62:609-13.

27. Cedergreen P, Swiatek F, Nielsen HB. Local anaesthesia for carotid endarterectomy Pro: protect the brain. Eur J Anaesthesiol 2016;33:236-7.

28. Stoneham MD, Stamou D, Mason J. Regional anaesthesia for carotid endarterectomy. Br J Anaesth 2015;114:372-83.

29. Singh SK. The cervical plexus: Anatomy and ultrasound guided blocks. Anaesth Pain Intensive Care 2015;19:323-32.

30. Pandit JJ, Satya-Krishna R, Gration P. Superficial or deep cervical plexus block for carotid endarterectomy: A systematic review of complications. Br J Anaesth 2007;99:159-69.

31. Beard J. Should all patients be shunted? If not, how can I predict which patients will require a shunt?# In: Naylor AR (ed). Carotid artery surgery. A problem based approach. London: WB Saunders; 2000. p. 244-247.

32. Counsell C, Salinas R, Naylor R, Warlow C. Routine or selective carotid artery shunting for carotid endarterectomy (and different methods of monitoring in selective shunting). Cochrane Database Syst Rev 2000:CD000190.

33. Halsey JH Jr. Risks and benefits of shunting in carotid endarterectomy. The International Transcranial Doppler laborators. Stroke 1992;23:1583-7.

34. Sundt TM Jr, Ebersold MJ, Sharbrough FW, Piepgras DG, Marsh WR, Messick JM Jr. The risk-benefit ratio of intraoperative shunting during carotid endarterectomy. Ann Surg 1986;203:196-204.

35. Evans WE, Hayes JP, Waltke EA, Vermilion BD. Optimal cerebral monitoring during carotid endarterectomy: neurologic response under local anesthesia. J Vasc Surg 1985;2:775-7.

36. Benjamin ME, Silva MB Jr, Watt C, McCaffrey MT, Burford-Foggs A, Flinn WR. Awake patient monitoring to determine the need for shunting during carotid endarterectomy. Surgery 1993;114:673-9.

37. Naylor AR. What evidence is there that regional anaesthesia confers any benifit over general anaesthesia? In: Naylor AR (ed). Carotid artery surgery. A problem based approach. London: WB Saunders; 2000. p. 205.

38. Ugurlucan M, Filik ME, Caglar IM, et al. Carotid endarterectomy using a "home-constructed" shunt for patients intolerant to cross-clamping. Surg Today 2015;45:284-9.

39. Siu A, Patel J, Prentice HA, Cappuzzo JM, Hashemi H, Mukherjee D. A Cost Analysis of Regional Versus General Anesthesia for Carotid Endarterectomy. Ann Vasc Surg 2017;39:189-94.

40. Hye RJ, Mackey A, Hill MD. Incidence, outcomes, and effect on quality of life of cranial nerve injury in the Carotid Revascularization Endarterectomy versus Stenting Trial. J Vasc Surg 2015;61:1208-14.

41. Kakisis JD, Antonopoulos CN, Mantas G, Moulakakis KG, Sfyroeras G, Geroulakos G. Cranial Nerve Injury After Carotid Endarterectomy: Incidence, Risk Factors, and Time Trends. Eur J Vasc Endovasc Surg 2017;53:320-35.

42. Naylor AR, Ricco JB. Response to Re: Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018;55:902.

43. Bowyer MW, Zierold D, Loftus JP, Egan JC, Inglis KJ, Halow KD. Carotid endarterectomy a comparison of regional versus general anesthesia in 500 operations. Ann Vasc Surg 2000;14:145-51.

44. McCarthy RJ, Walker R, McAteer P, Budd JS, Horrocks M. Patient and Hospital Benefits of Local Anaesthesia for Carotid Endarterectomy. Eur J Vasc Endovasc Surg 2001;22:13-8.

45. Bowyer MW, Zierold D, Loftus JP, Egan JC, Inglis KJ, Halow KD. Carotid endarterectomy: a comparison of regional versus general anesthesia in 500 operations. Ann Vasc Surg 2000;14:145-51.

46. Sternbach Y, Illig KA, Zhang R, et al. Hemodynamic benefits of regional anesthesia for carotid endarterectomy. J Vasc Surg 2002;35:333-9.

47. Mofidi R, Nimmo AF, Moores C, Murie JA, Chalmers RT. Regional versus general anaesthesia for carotid endarterectomy: impact of change in practice. Surgeon 2006;4:158-62.

48. Gürer O, Yapıcı F, Yapıcı N, Özler A, Işık Ö. Comparison between local and general anesthesia for carotid endarterectomy: early and late results. Vasc Endovascular Surg 2012;46:131-8.

49. Kalko Y, Kafali E, Aydin U, et al. Surgery of the Carotid Artery : Local anaesthesia versus general anaesthesia. Acta Chir Belg 2007;107:53-7.

50. McCarthy RJ, Walker R, McAteer P, Budd JS, Horrocks M. Patient and hospital benefits of local anaesthesia for carotid endarterectomy. Eur J Vasc Endovasc Surg 2001;22:13-8.

51. GALA Trial Collaborative Group; Lewis SC, Warlow CP. General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial. Lancet 2008;372:2132-42.

52. Bonati LH, Fraedrich G; Carotid Stenting Trialists' Collaboration. Age modifies the relative risk of stenting versus endarterectomy for symptomatic carotid stenosis--a pooled analysis of EVA-3S, SPACE and ICSS. Eur J Vasc Endovasc Surg 2011;41:153-8.

53. Pennekamp CW, Immink RV, den Ruijter HM, et al. Near infrared spectroscopy to indicate selective shunt useduring carotid endarterectomy. Eur J Vasc Endovasc Surg 2013;46:397-403.

54. Chou EL, Sgroi MD, Chen SL, Kuo IJ, Kabutey NK, Fujitani RM. Influence of gender and use of regional anesthesia on carotid endarterectomy outcomes. J Vasc Surg 2016;64:9-14.

55. Vaniyapong T, Chongruksut W, Rerkasem K. Local versus general anaesthesia for carotid endarterectomy. Cochrane Database Syst Rev 2013:CD000126.

56. Hussain AS, Mullard A, Oppat WF, Nolan KD. Increased resource utilization and overall morbidity are associated with general versus regional anesthesia for carotid endarterectomy in data collected by the Michigan Surgical Quality Collaborative. J Vasc Surg 2017;66:802-9.

57. Leichtle SW, Mouawad NJ, Welch K, Lampman R, Whitehouse WM Jr, Heidenreich M. Amerikan Cerrahi Koleji Ulusal Cerrahi Kalite Geliştirme Programı'ndan genel ve bölgesel anestezi altında karotis endarterektomi sonuçları. J Vasc Surg 2012;56:81-3.

58. Ugurlucan M, Akay HT, Erdinc I, et al. Anticoagulation strategy in patients with atrial fibrillation after carotid endarterectomy. Acta Chir Belg 2018:1-8.

E Journal of Cardiovascular Medicine
Research Article
9
EJCM 2019;7(1):9-15
DOI: 10.32596/ejcm.galenos.2019.00050

A Research for Predictive Value of Hemogram Parameters at Late Term Arteriovenous Fistula Thrombosis Formation

Gökmen Akkaya, Çağatay Bilen

Ege University Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Turkey

Abstract

Objectives: This study aims to assess the relation between late term arteriovenous fistula thrombosis and alteration in hemogram parameters before the occurrence of thrombosis in hemodialysis patients with end-stage renal failure.

Materials and Methods: Data of three hemodialysis centers in our city were evaluated retrospectively. The results of hemogram values before thrombosis formation at first and third month in 14 re-operated patients between March-September 2017, owing to late term fistula thrombosis occurrence, who previously had a successful fistula access, were compared to 73 patients still having hemodailysis therapy via fistula access.

Results: Statistically significant increments were measured in neutrophile to lympocyte ratio, red blood cell distribution width, mean platelet volume, platelet distribution width parameters in fistula thrombosis developed patients compared to their previous results three months before thrombosis formation and control group. No significant relation was found between thrombosis formation and other parameters in hemogram.

Conclusion: Herein, it's determined that a profound examination of hemogram has a predictive value for late term fistula thrombosis in hemodialysis patients.

Keywords: Fistula thrombosis, hemogram, neutrophile tolympocyte ratio, red blood cell distribution width, mean platelet volume, platelet distribution width

Address for Correspondence: Gökmen Akkaya, Ege University Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Turkey
Phone: +90 506 861 00 84 **e-mail:** akkayagokmen@gmail.com **ORCID ID:** orcid.org/0000-0002-0509-1971
Received: 04.11.2018 **Accepted**: 11.02.2019

Cite this article as: Akkaya G, Bilen Ç. A Research for Predictive Value of Hemogram Parameters at Late Term Arteriovenous Fistula Thrombosis Formation. EJCM 2019;7(1):9-15.
DOI: 10.32596/ejcm.galenos.2019.00050

Introduction

Nowadays, with the advances in healthcare and prolonged life expectancy, there has been an increase in end-stage renal disease patients (ESRDP)[1]. In this patient population, autogenous arteriovenous fistula (AVF), which has been created to provide hemodialysis, should be considered as the first choice for vascular access due to its long-term patency, increased patient comfort and low complication rate[2]. Complications of vascular access in these patients may cause morbidities therefore patency of an AVF that provides an adequate flow (300-400 mL/min) is crucial[3].

Although early stage thrombosis due to AVF is often associated with surgical complications and technique, success for vascular access at one-year postoperatively varies between 42% and 90%, depending on various reasons[4]. As for the cause of thrombosis formation in the late period, neointimal hyperplasia and inflammatory processes are the most common reasons[5]. Therefore, many enzymes, hormones and biochemical parameters have been studied so as to identify a predictive marker before the occurrence of thrombosis[5-8].

The hemogram is an inexpensive and fast test that provides extensive information which is frequently utilized in ESRDP. In recent articles, especially, neutrophil to lymphocyte ratio (NLR) and red cell distribution width (RDW) are often associated with inflammatory processes and secondary thrombotic processes[9,10].

In this study, the data of patients who were operated on for late AVF thrombosis and who were receiving routine hemodialysis via AVF were analyzed retrospectively and the relation between AVF stenosis and haemogram parameters was investigated.

Materials and Methods

For this study, the data of three separate hemodialysis centers in Şırnak province were retrospectively reviewed. Overall 96 patients receiving hemodialysis treatment were evaluated. The case group consisted of 14 patients referred to us from these three centers, whom were afterwards operated on in our institute due to late-onset fistula thrombosis and between March and September 2017. Heretofore, all patients were successfully receiving hemodialysis treatment via AVF.

The patients who had fistula thrombosis in less than a month following AVF opening, or who were still not able to receive a successful hemodialysis treatment with fistula access a month after the AVF opening, were excluded in the study. On the other hand, the control group was comprised of 73 patients who were receiving hemodialysis treatment with AVF access. A total of 87 patients were included in this study. Nonetheless, nine patients undergoing hemodialysis treatment via catheter were not included in any group.

Routine hemogram examines at monthly intervals of these patients at all three centers has being done by the devices of same brand and model (Siemens, Sysmex XT 1800i, Germany).

The device calibrations are supervised by the same biochemistry specialist. Thus, the differences originating from measurement errors among the hemogram values were minimized. Hemogram values were recorded before the thrombosis development at first and third months from the patients who had late fistula thrombosis. In control group, the results of the hemogram which are performed in the last month were evaluated. Case group value at month one recorded as 1A and the third month group was 1B. The control group was named as group 2 and the statistical analysis was performed.

Statistical Analysis

Statistical Package for Social Sciences Package (SPSS-Chicago, IL, USA) 15.0 programme was used for statistical analysis. The quantitative data was evaluated with chi-square test. Kolmogorov-Smirnov test was used to determine the normal distribution of the variables. Parametrical data analysis was performed by ANOVA instead of Student t-test, as the case group was divided into two subgroups that including the results belonging to 1st and 3rd months. Post-hoc test was utilized to significant p

values after ANOVA. Paired comparisons were made with Bonferroni Test because of different sample sizes between groups. P value <0.05 was considered as statistically significant.

Informed consent form was obtained from each patient before surgical process.

Results

A total of 14 fistula patients with AVF thrombosis, had undergone initial AVF opening operations at different dates by various surgeons. Thirteen (92.8%) radiocephalic and one (7.2%) brachiocephalic anastomosis was performed to those. Nine (64.2%) of the radiocephalic fistulas were located at the wrist level (Brescia-Cimino) and 4 (28.5%) were at the Snuffbox zone. Except for two (14.2%) Brescia-Cimino fistulas, all Brescia-Ciminofistulas were locating in the left arm. AVF thrombosis occurred in three patients following second AVF opening, and in one, following the third attempt. Previously, all patients were successfully receiving hemodialysis treatment via AVF access. Mean time between AVF opening and thrombosis occurrence was 9 (3-28) months.

Brescia-Cimino fistula was performed in 3 patients in the same forearm with the Snuffbox fistula thrombosis. Among the 9 patients with Brescia-Cimino fistula, three patients underwent thrombectomy, three patients underwent radiocephalic fistula operation at a more proximal level (one of which had developed an early fistula in the 48 hours after thrombectomy). Brachiocephalic AVF was opened to two patients in the same limb and for the other two patients, Brescia-Cimino fistula was created from the other forearm due to multiple and large venous aneurysms. In addition to these, one patient had brachiocephalic AVF from the other arm due to the previous surgical deliveries.

Demographic data such as age, gender and presence of comorbidities were compared with the control group and no significant difference was determined (Table 1).

Hemogram values of the first and third months of the patients before fistula thrombosis occurrence and the patients comprising the control group while receiving hemodialysis via fistula uneventfully were compared. Only four parameters were determined as statistically significant in triple group analysis. Those were RDW (p=0.02), platelet distribution width (PDW), (p=0.04); mean platelet volume (MPV), (p=0.02) and NLR (p=0.01) respectively (Table 1). Bonferroni pairwise comparison test was then applied to aforementioned four parameters to distinguish the significant values. When the results of the case group for first month was considered, there was a significantly difference in comparisons with to their third month measurements before thrombosis formation as well as the control group values. However, the third month and the control group values did not differ in paired analysis.

The values were calculated as p=0.011, p=0.016 for RDW; p=0.021, p=0.034 for PDW, p=0.018, p=0.026 for MPV and p<0.001, p<0.001 for NLR; respectively (Table 2). There was no statistically significant difference between the other paired comparisons.

Discussion

In this study, four different hemogram parameters were detected that may associate with late term AVF thrombosis. NLR, RDW, PDW, MPV values one month before the thrombosis formation showed an increment when compared with the results of either their values at the third month before thrombosis or control group. Moreover, these outcomes were determined as statistically significant.

There are several studies investigating the physiopathology that underlying AVF thrombosis formation. In the literature, numerous biochemical markers which are frequently used in daily routine have been investigated in order to determine a predictive influence on this issue.

Morton et al. have evaluated 1512 patients from thirteen different studies in their meta-analysis study[11]. At the end of the study, no relation was found between AVF thrombosis development and a total of twelve biochemical parameters including hemoglobin levels and C-reactive

protein (CRP). In contrast to this, Chou et al. designed a study considering the hypothesis that CRP increment is accelerating the neointimal hyperplasia among 51 AVF thrombosis developed patients and determined an association between CRP values and AVF thrombosis formation[12]. A similar result was also stated by Kuo et al.[13].

Studies investigating the relationship between AVF thrombosis and the inflammatory process are not limited to CRP. In addition to NLR, RDW is also associated with inflammatory process and assessed in various studies concerning the AVF thrombosis formation. Çiçek et al. have examined the relationship between preoperative NLR and fistula success in a serial of 80 patients from three different centers in their study[14]. Consequently, they concluded that an alteration at NLR may be a guide for the treatment and prognosis of AVF thrombosis. Furthermore, Usman et al. determined that NLR and RDW values are associated with the development of fistula thrombosis in their study that consists of 150 patients[15]. These outcomes have been corroborated by Bojakowski et al.[16]. They conducted a retrospective study aiming to determine the potential risk factors for late term AVF thrombosis and found RDW and NLR values directly related.

Therewithal, similar results for RDW and NLR were found to be significant in terms of early fistula thrombosis. Memetoğlu et al. indicate that RDW and

Table 1. Comparison of demographic data and hemogram values between groups

		Patients	Group 1A (before AV fistula thrombosis month 1)	Group 1B (before AV fistula thrombosis month 3)	Group 2	p value
Number		87	14		73	0.32
Age		62±14	64±12		60±15	0.14
Gender	F	36 (41.3%)	6 (42.8%)		30 (47.6%)	0.52
	M	41 (58.7%)	8 (57.2%)		33 (53.4%)	0.68
Diabetes		27 (31%)	6 (42.8%)		21 (28.7%)	0.07
Hypertension		69 (79.3%)	11 (78.5%)		58 (78.4%)	0.92
Cigarette (pack year)		48±24	46±18		49±22	0.23
Hyperlipidemia		29 (34.5%)	5 (35.7%)		25 (34.2%)	0.83
Hemogram values						
WBC (10^9/L ± SD)		7.2±2.2	8.2±2.1	7.6±1.7	7.5±2.3	0.06
RBC (x10^{12}/L ± SD)		3.7±0.4	3.6±0.5	3.6±0.8	3.7±0.6	0.22
Hb (g/dL ± SD)		10.9±1.2	11.1±0.7	11.0±0.6	10.9±1.0	0.17
HCT (%, ± SD)		32.8±3.7	33.2±3.1	33.0±2.9	32.7±4.6	0.08
PLT (x10^3/μL ± SD)		242±91	236±102	240±106	243±89	0.06
MCH (fL ± SD)		30.6±2.4	30.3±2.5	31.1±2.2	30.4±1.8	0.34
MCHC (q/dL±SD)		32.4±1.0	32.7±0.8	32.5±1.1	32.2±1.7	0.19
MCV (fL ± SD)		87.3±8.2	86.9±10.1	87.2±8.0	87.5±9.2	0.14
RDW (fL ± SD)		44.5±6.3	47.2±7.2	44.2±6.2	44.5±5.9	0.02*
PDW (fL ± SD)		13.6±2.8	14.3±2.6	13.4±3.0	13.5±2.5	0.04*
MPV (fL ± SD)		11.2±0.9	12.1±1.2	11.4±0.8	11.2±1.1	0.02*
Neutrophils (10^9/L ± SD)		6.4±2.6	7.2±3.0	6.6±2.4	6.3±2.7	0.08

WBC: White blood cell, RBC: Red blood cell, Hb: Hemoglobin, HCT: Hematocrit, PLT: Platelet, MCH: Mean corpuscular hemoglobin, MCHC: Mean erythrocyte hemoglobin concentration, RDW: Red cell distribution width, PDW: Platelet distribution width, MPV: Mean platelet volume, AV: Arteriovenous, MCV: Mean cell volume, SD: Standard deviation, F: Female, M: Male, data are presented as mean ± standard deviation or as number and percentage. Statistical analysis performed with chi-square test
**Statistically significant results are written in bold*

Table 2. Paired comparisons with the bonferroni test of the parameters that calculated significant at ANOVA test

			Averages difference	Standard deviation	p value	95% security range	
						Lower limit	Upper limit
RDW	Group 1A	Group 1B Group 2	3.0 2.8	3.004 3.015	0.011 0.016	0.4 0.5	6.1 5.8
	Group 1B	Group 1A Group 2	-3.0 -0.3	3.004 3.063	0.011 0.810	-6.1 -3.3	-0.4 2.6
	Group 2	Group 1A Group 1B	-2.8 0.3	3.015 3.063	0.016 0.810	-5.8 -2.6	-0.5 3.3
MPV	Group 1A	Group 1B Group 2	0.7 0.9	3.021 3.046	0.021 0.034	0.4 0.5	1.1 1.2
	Group 1B	Group 1A Group 2	-0.7 0.2	3.021 3.014	0.021 0.243	-1.1 -0.1	-0.4 0.5
	Group 2	Group 1A Group 1B	0.9 -0.2	3.046 3.014	0.034 0.243	-1.2 -0.5	-0.5 0.1
PDW	Group 1A	Group 1B Group 2	0.9 0.8	3.148 3.042	0.018 0.026	0.4 0.5	1.3 1.2
	Group 1B	Group 1A Group 2	-0.9 -0.1	3.148 3.073	0.018 0.948	-1.3 -0.5	-0.4 0.3
	Group 2	Group 1A Group 1B	-0.9 0.1	3.042 3.073	0.026 0.948	-1.3 0.3	-0.4 0.5
NLR	Group 1A	Group 1B Group 2	0.77 0.70	3.002 3.006	0.000 0.000	0.46 0.35	1.08 0.96
	Group 1B	Group 1A Group 2	-0.77 -0.07	3.002 3.314	0.000 0.634	-1.08 0.25	0.46 0.39
	Group 2	Group 1A Group 1B	-0.70 0.07	3.006 3.314	0.000 0.634	-0.96 -0.39	-0.35 -0.25

RDW: Red cell distribution width, PDW: Platelet distribution width, MPV: Mean platelet volume, NLR: Neutrophile to lympocyte ratio

NLR values are associated with rapidly developing AVF thrombosis and they remark that these parameters may have a cautionary value[17]. Despite several hemogram parameters were examined in these studies, the PDW and MPV parameters which are related to platelets were not evaluated. However, we had a change to measure these parameters and the results were found as statistically significant.

Although the increase in MPV and PDW are often associated with thrombotic and inflammatory processes; in literature search, no reports were found considering the patients with the AVF thrombosis. Thus, as per our knowledge, our recent study has to be a feature of being the first study concerning this issue. Besides that, there are several publications on the relationship between these parameters and cardiovascular diseases[18-21]. In their meta-analysis study, Chu et al. determined a significant association between MPV increase and acute myocardial infarction and other cardiovascular diseases[20]. Therefore, they defined MPV as a prognostic indicator and a risk factor.

There are limited studies investigating PDW. De Luca et al. have determined no significant relationship between coronary artery disease and PDW in a prospective study involving 1882 patients[21]. On the other hand, in a study containing 53 patients with cerebral venous sinus thrombosis, Kamışlı et al. found significant increase in MPV and PDW values and therefore suggest that these parameters may be thought as predictive markers[22].

Consistently with the literature in this study, the NLP, MPV, PDW and RDW parameters which are associated

with inflammatory and prothrombotic processes in prior studies were found to be compatible with late stage AVF thrombosis. The increase between first and third month values before the development of thrombosis was determined as significant. However, no significant difference was evaluated between third month values and control group results in paired comparisons. In the light of these results, we are in opinion that the increase aforementioned parameters may be interpreted in favor of thrombosis development.

Retrospective design, limited patient population and the opening of the initial AVFs by different surgeons constitute the limitations of this study. Further randomized, prospective studies in larger series are needed to support this data.

To summarize, an increase in PDW, MPV, NLP and RDW parameters in a regular and profound hemogram examination has a predictive value and may provide a clinical benefit for AVF thrombosis formation in patients who were receiving hemodialysis via AVF with the diagnosis of end-stage renal failure.

Ethics

Ethics Committee Approval: Due to the retrospective design of the study, the ethical approval did not obtained.

Informed Consent: Informed consent form was obtained from each patient before surgical process.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.A., Ç.B., Concept: G.A., Design: G.A., Ç.B., Data Collection or Processing: G.A., Ç.B., Analysis or Interpretation: Ç.B., Literature Search: Ç.B., Writing: G.A., Ç.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Başel H, Çeğin, MB, Aydın, Ü, et al. A Diyaliz amacı ile oluşturulan arteriyovenöz fistül operasyonu sonrası gelişen komplikasyonlar ve buna fistü laçım yerinin etkisi. Van Tıp Dergisi, 2010;17:118-23.
2. Murphy GJ, White SA, Nicholson ML, Vascular access for haemodialysis. Br J Surg 2000;87:1300-15.
3. Konner K, Nonnast-Daniel B, Ritz E, The arteriovenous fistula. J Am SocNephrol 2003;14:1669-80.
4. Allon M, Robbin ML, Increasing arteriovenous fistulas in hemodialysis patients: problems and solutions. Kidney Int 2002;62:1109-24.
5. Roy-Chaudhury P, Khan R, Campos B, et al. Pathogenetic role for early focal macrophage infiltration in a pig model of arteriovenous fistula stenosis. J Vasc Access 2014;15:25-8.
6. Lippi, G, Targher, G, Montagnana, M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Archives of pathology & laboratory medicine, 2009;133:628-32.
7. Arbel, Y, Finkelstein A, Halkin A, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis, 2012;225:456-60.
8. Marrone D, Pertosa G, Simon M, et al. Local activation of interleukin 6 signaling is associated with arteriovenous fistula stenosis in hemodialysis patients. American Journal of Kidney Diseases, 2007;49:664-73.
9. Taşoğlu İ, Turak O, Nazli Y, et al Preoperative neutrophil-lymphocyte ratio and saphenous vein graft patency after coronary artery bypass grafting. Clinical and Applied Thrombosis/Hemostasis, 2014;20:819-24.
10. Förhécz Z, Gombos T, Borgulya G, et al, Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, in- flammation, renal function, and nutritional state. Am Heart J 2009;158:659-66.
11. Morton SK, Rodríguez AJ, Morris DR, et al. Systematic Review and Meta-Analysis of Circulating Biomarkers Associated with Failure of Arteriovenous Fistulae for Haemodialysis. PLoS One. 2016:26;11 e0159963.
12. Chou CY, Kuo HL, Yung YF, et al, C-reactive protein predicts vascular access thrombosis in hemodialysis patients. Blood purification, 2006;24:342-6.
13. Kuo WH, Lee YT, Nang HY, et al, C-reactive protein variability is associated with vascular access outcome in hemodialysis patients. J Clin Lab Anal 2017 Apr 27
14. Çiçek MC, Çiçek ÖF, Özkan T, et al. PreoperatifNötrofil/LenfositOranınınErkenDönemArterio-VenözFistülBaşarısındakiPrognostikÖnemi. UluslararasıKlinikAraştırmalarDergisi2014;2:31-34.
15. Usman R, Jamil M, Naveed M, High Preoperative Neutrophil-Lymphocyte Ratio (NLR) and Red Blood Cell Distribution Width (RDW) as Independent Predictors of Native Arteriovenous Fistula Failure. Annals of Vascular Diseases, 2016;5:157-60.
16. Bojakowski K, Dzabic M, Kurzejamska E, et al. "A high red blood cell distribution width predicts failure of arteriovenous fistula." PloS one 7.5 (2012): e36482.

17. Memetoğlu ME, Yilmaz M, Kocaaslan C, et al. Red blood cell distribution width is associated with early failure of arteriovenous fistula for haemodialysis access. Blood Coagulation & Fibrinolysis, 2015;26:32-35.

18. Gasparyan Y, Ayvazyan L, Mikhailidis D, et al. Mean platelet volume: a link between thrombosis and inflammation?. Current pharmaceutical design, 2011;17:47-58.

19. Sakallı H, Baskın E, Bayrakçı US, et al Mean platelet volume as a potential predictor of renovascular thrombosis after renal transplant. ExpClin Transplant, 2013;11:27-31.

20. Chu SG, Becker RC, Berger PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. J ThrombHaemost. 2010;8:148-56.

21. De Luca G, Venegoni L, Iorio S, et al. Atherosclerosis Study Group. Platelet distribution width and the extent of coronary artery disease: results from a large prospective study. Platelets, 2010;21:508-14.

22. Kamisli O, Kamisli S, Kablan Y, et al. The prognostic value of an increased mean platelet volume and platelet distribution width in the early phase of cerebral venous sinus thrombosis. Clinical and Applied Thrombosis/ Hemostasis, 2013;19:29-32.

Research Article

E Journal of Cardiovascular Medicine

EJCM 2019;7(1):16-21

DOI: 10.32596/ejcm.galenos.2019.00003

Tranexamic Acid, a Low-cost and Practical Hemostatic Agent Against Diffuse Microvascular Bleeding Due to Coagulopathy in Heart Surgery

Kenan Abdurrahman Kara[1], Hakan Öntaş[2]

[1]Yeditepe University Hospital, Department of Cardiovascular Surgery, İstanbul, Turkey
[2]Balıkesir Atatürk City Hospital, Clinic of Cardiovascular Surgery, İstanbul, Turkey

Abstract

Objectives: Bleeding after open heart surgery is an important cause of morbidity and mortality. It may not always be related to surgical bleeding. Bleeding due to coagulopathy, called diffuse microvascular bleeding, is more commonly seen in the post-operative period. The objective of this study is to assess the effect of administering transamine, which we consider a low-cost and effective hemostatic agent, during open heart surgery on post-operative bleeding amount, blood product use, length of stay in intensive care, and duration of hospitalization.

Materials and Methods: A total of 24 patients were enrolled in the study at the Hisar Intercontinental Hospital between March 2017-December 2017. 12 patients were administered tranexamic acid 10% 500 mg I.V. before starting sternal incision for open heart surgery. 10% 500 mg I.V. tranexamic acid dose was repeated during separation from the heart-lung machine at the end of the operation. The other 12 patients were followed-up as a control group. Patients were followed-up for drainage in the post-operative period. The patients were monitored for re-operation due to bleeding and significant side effects. Bleeding amounts and re-operation rates were compared.

Results: When the results from the two groups were evaluated, revision rates, amounts of used blood and blood products, total drainage amount were less, and stay in intensive care and discharge time were shorter in the group given tranexamic acid.

Conclusion: We think that tranexamic acid, which is used as a low-cost and effective pharmacological agent in heart surgery, will significantly reduce post-operative bleeding and the need for blood transfusion in patients undergoing heart surgery.

Keywords: Tranexamic acid, diffuse microvascular bleeding, coagulopathy after CABG, re-operation

Address for Correspondence: Kenan Abdurrahman Kara, Yeditepe University Hospital, Clinic of Cardiovascular Surgery, İstanbul, Turkey
Phone: +90 530 065 52 25 **e-mail:** kenankaradoc@gmail.com **ORCID ID:** orcid.org/0000-0003-1295-7689
Received: 02.02.2019 **Accepted**: 21.02.2019

Cite this article as: Kara KA, Öntaş H. Tranexamic Acid, a Low-cost and Practical Hemostatic Agent Against Diffuse Microvascular Bleeding Due to Coagulopathy in Heart Surgery. EJCM 2019;7(1):16-21.
DOI: 10.32596/ejcm.galenos.2019.00003

Introduction

Open heart surgeries bring out the need for blood and blood products[1]. Although heart surgeons avoid the use of blood and blood products, these are usually used in the post-operative period. Post-operative excessive blood loss can progress to anemia, hemodynamic changes, re-operation, and even mortality. Immunologic, metabolical and endocrinologycal disorders may develop as a result of post-operative excessive bleeding[2]. Moreover, excessive amount of blood transfusion during treatment may cause several complications. These include immunological reactions, anaphylaxis, sepsis and risk of viral infection transmission[2-4]. Blood transfusions carry a risk of complications such as fever, hemolytic reaction, allergic reaction, citrate toxicity, air embolism as well as transmitting blood-borne diseases (viral hepatitis, HIV, malaria, infectious mononucleosis and cytomegalovirus infections)[5]. When we evaluate these complications, the importance of surgical bleeding control during open heart surgery becomes evident. However, no matter how carefully a surgeon controls the bleeding, sometimes bleeding cannot be prevented due to factors affecting coagulopathy. Coagulopathy causing such types of bleeding seen after open heart surgery is a frequent problem. It may be observed depending on several factors such as thrombocytopenia, platelet function disorder, loss of clotting factors, increased amount of free heparin[6-8]. In the studies conducted, 5-25% life-threatening bleeding were seen in patients undergoing open heart surgery with cardiopulmonary bypass (CPB)[9,10], and 2-7% of patients required re-operation due to bleeding[3,11,12]. Re-operation in patients causes outcomes such as prolonged mechanical ventilation support, increased inotropic support, increased stay in intensive care, hypothermia caused by connecting to the heart-lung machine again, and coagulopathy. This considerably increases morbidity, mortality and hospital costs. Bleeding due to coagulopathy was detected in 50-80% of patients undergoing re-operation, rather than surgical bleeding[13]. During the re-operation, bleeding control performed by the surgeon generally cannot find an active bleeding focus and usually cauterizes the micro-bleeding focus leaking from the tissues. This suggests that the bleeding is related to an acute acquired hemostatic disorder. This clinical picture, called diffuse microvascular bleeding, is a coagulation disorder depending on many factors. Contributing factors to this picture are consumption of coagulation factors, platelet function disorder, rebound effect of heparin, excessive fibrinolysis, low platelet count, excessive heparin and protamine, complement activation and disseminated intravascular coagulation[10-12]. The most frequent factors among these are excessive fibrinolysis (25-45%) and platelet function disorder[2,3,14,15,19]. Various pharmacological agents have been used in recent years to reduce excessive bleeding during open heart surgery. Tranexamic acid, aprotinin, desmopressin and prostacyclins are among these pharmacological agents. Tranexamic acid is a synthetic hemostatic agent with antifibrinolytic activity. It inhibits the activity of plasminogen activators and plasmine[16-18,20]. In this study, we compared the bleeding amounts of two groups of patients in the post-operative period after open heart surgery, with and without intravenous administration of tranexamic acid.

Materials and Methods

The objective was to compare the effect of tranexamic acid on post-operative bleeding.

Twenty four patients underwent an isolated coronary artery bypass graft operation using CPB by a single surgeon between March 2017-December 2017 at the Hisar Intercontinental Hospital. In 12 patients (10 males, 2 females; mean age: 57.16) open heart surgery was started with routine heparinization. Neutralization was performed with protamine to weane the patient from the heart-lung machine. Twelve patients (8 males, 4 females; mean age: 56.25) were administered 10% 500 mg I.V. before starting sternal incision for open heart surgery. 10% 500 mg I.V. tranexamic acid dose was repeated during separation from the heart-lung machine at the end of the operation. Patients were followed-up for drainage in the post-operative

period. Bleeding amounts and re-operation rates were compared. The other 12 patients were followed-up as a control group, and transaminic acid was not administered. Extubation hours, drainage amounts, re-operation due to bleeding, withdrawal time of chest tubes, length of stay in intensive care and discharge time were reviewed.

Surgery was performed through a median sternotomy with cardiopulmonary bypass established through right atrial and ascending aortic cannulation. Intermittent cold cardioplegia was used in the initial 24 patients and blood cardioplegia thereafter. An intravenous second-generation cephalosporin antibiotic was administered intraoperatively and for 48 hours postoperatively for prophylaxis against infection.

Patients who were diabetic or had renal failure or experienced any cerebrovascular events were excluded from the study.

The most important limitation of this study was the small number of patients.

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

The approval was obtained by the Yeditepe University Ethics Committee for this study (number: 13.02.2019/966). Written informed consent was obtained from the patients.

Results

In all patients enrolled, pre-operation hemoglobin, hematocrit, platelet count, prothrombine time, active partial thromboplastine time were within normal limits. There was no difference between the cases included in the study. All patients were discharged without any problems following operation.

When the results from the two groups were evaluated, revision rates, amounts of used blood and blood products, total drainage amount were less, and stay in intensive care and discharge time were shorter in the group given tranexamic acid (Table 1, Table 2, Table 3).

In the patient group receiving tranexamic acid systemically, the mean total amount of drainage was

Table 1. Operative and post-operative data of patients tranexamic acid group

Procedure	ICU (day)	Hospital (day)	Drainage (mL)	Age/gender	Used blood products
1-cabgx3	2	7	800	74/M	2 ES
2-cabgx3 + CE	3	6	900	63/M	3 ES
3-cabgx3	2	7	700	54/M	1 ES
4-cabgx4	2	5	800	64/M	2 ES
5-cabgx3	2	5	750	42/M	2 ES
6-cabgx3	2	8	650	61/F	2 ES
7-cabgx4	2	7	800	55/M	3 ES
8-cabgx3	3	7	900	55/F	1 ES
9-cabgx3	2	8	700	66/F	1 ES
10-cabgx3	2	7	700	62/M	1 ES
11-cabgx3	3	7	800	70/M	2 ES
12-cabgx3	2	7	700	64/F	2 ES
Mean	2.25	6.75	775	56.25	1.83 ES

CE: Carotid endarterectomy, cabg: Coronary artery bypass grafting, ICU: Intensive care unit, M: Male, F: Female, ES: Erytrocyte

775 mL, and the mean amount of used blood and blood products was 1.83 units of erythrocyte while in the patients not given tranexamic acid systemically, the mean amount of drainage was 850 mL and the mean amount of used blood and blood products was 2.5 units of erythrocyte and a total of 2 units of platelets following the operation. One patient in the group not administered tranexamic acid was retaken into the operation room from intensive care unit for bleeding revision 4 hours after the end of the operation. No surgical foci were detected during the bleeding control performed on the patient. The bleeding foci in the form of leakage were cauterized. The patient was then submitted back to intensive care.

Table 2. Measured pre-operative and per-operative variables of 24 patients

Hypertension	18
Peripheral vascular disease	2
IABP insertion	1
Emergent surgery	1
Hyperlipidemia	18
History of smokin	20
Respiratory failure	0
Reexploration for bleeding	1
COPD	14

IABP: Intra-aortic balloon pump, COPD: Chronic obstructive pulmonary disease

Discussion

Surgical bleeding seen in some of the patients after open heart surgery can be stopped with an re-intervention. However, sometimes a disseminated and heavy bleeding may be observed, suggesting a disorder in the hemostatic system. These kinds of bleeding may be seen due to thrombocytopenia, reduction of clotting factors, increase of fibrinolysis, excessive heparinization, insufficient heparin neutralization, and the rebound effect of heparin. Giving excessive amounts of protamine as well as insufficient heparin neutralization may have side effects on the cardiovascular system. In the study conducted, tranexamic acid was administered to heart surgery patients at risk of high transfusion[16]. It was observed that the blood product use and drainage amounts in patients who were administered tranexamic acid were reduced[17].

Tranexamic acid is known to have topical applications in addition to its systemic use. Its administration into the pericardial cavity in patients undergoing elective coronary artery bypass surgery was reported to significantly reduce the post-operative blood loss and the need for transfusion and to block side effects[10]. Fawyz et al. reported that topical application of tranexamic acid for bleeding control following open heart surgery reduced post-operative blood

Table 3. Operative and post-operative data of patients without tranexamic acid

Procedure	ICU (day)	Hospital (day)	Drainage (mL)	Age/gender	Used blood products
1-cabgx4	2	8	900	48/M	3 ES,1 thromb
2-cabgx3	2	6	850	56/M	3 ES
3-cabgx3	3	7	850	52/M	2 ES
4-cabgx3	2	8	800	58/M	2 ES
5-cabgx2	3	8	850	49/M	2 ES
6-cabgx3	2	8	800	68/M	2 ES
7-cabgx4	3	7	900	48/M	4 ES,1 thromb
8-cabgx3	2	7	800	57/M	2 ES
9-cabgx3	3	7	900	60/F	3 ES
10-cabgx2	3	7	800	62/F	2 ES
11-cabgx2	2	7	900	68/M	2 ES
12-cabgx3	3	7	900	60/M	3 ES
Mean	2.5	7.25	850	57.16	2.5 ES + 2 thromb

ICU: Intensive care unit, cabg: Coronary artery bypass grafting, M: Male, F: Female, ES: Erytrocyte

loss and that it did not pose any risks for the patient[21-23]. Another study by Abdul-Azm et al. demonstrated that the use of topical tranexamic acid reduced post-operative mediastinal bleeding and reexploration[24]. It was reported that administration of tranexamic acid at various doses during the operation reduced blood loss and the need for transfusion but it did not have any long-term benefits. It was also shown that administering a low dose of tranexamic acid after coronary artery bypass surgery significantly reduced the bleeding amount and the need for blood transfusion[25-27].

All patients who are followed up after angio stent procedure into heart surgery or with a congenital adrenal hyperplasia diagnosis already use routine acetylsalicylic acid or clopidogrel and, in some cases, other drugs such as tirofiban or ticagrelor, which have a high risk of bleeding. Development of bleeding diathesis is also quite high in these patients with a history of using these medicines. When all these strong medicines affecting the coagulation cascade are evaluated, a simple administration of tranexamic acid alone is of course not enough for bleeding control. However it has a non-negligible beneficial effect in terms of economy and effectiveness, as shown in this study[28-30].

Based on the study we performed, we think that systemic use of tranexamic acid relatively causes a decrease in post-operative bleeding amount and the amounts of used blood transfusions and blood products compared to the control group. However, the most important limitation of this study was the small number of patients studied.

We think that tranexamic acid, which we administered before incision in the per op period and after the operation, is a quite simple, practical and economic hemostatic agent. Tranexamic acid significantly reduces post-operative bleeding and blood transfusion requirement in heart surgery patients. In conclusion, systemic use of tranexamic acid in open heart surgery caused a decrease in post-operative bleeding amount without producing any side effects.

Ethics

Ethics Committee Approval: The approval was obtained by the Yeditepe University Ethics Committee (number: 13.02.2019/966).

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.A.K., Concept: K.A.K., Design: K.A.K., Data Collection or Processing: K.A.K., H.Ö., Analysis or Interpretation: K.A.K., H.Ö., Literature Search: K.A.K., H.Ö., Writing: K.A.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Yeh T Jr, Shelton L, Yeh TJ. Blood loss and bank blood requirement in coronary bypass surgery. Ann Thorac Surg 1978;26:11-6.
2. Huang H, Ding W, Su Z, Zhang W. Mechanism of the preserving effect of aprotinin on platelet function and its use in cardiac surgery. J Thorac Cardiovasc Surg 1993;106:11-8.
3. Casati V, Guzzon D, Oppizzi M, et al. Tranexamic acid compared with high-dose aprotinin in primary elective heart operations: effects on perioperative bleeding and allogeneic transfusions. J Thorac Cardiovasc Surg 2000;120:520-7.
4. Mongan PD, Brown RS, Thwaites BK. Tranexamic acid and aprotinin reduce postoperative bleeding and transfusions during primary coronary revascularization. Anesth Analg 1998;87:258-65.
5. Zuck TF. Transfusion-transmitted AIDS reassessed. N Engl J Med 1988;318:511-2.
6. Kucuk O, Kwaan HC, Frederickson J, Wade L, Green D. Increased fibrinolytic activity in patients undergoing cardiopulmonary bypass operation. Am J Hematol 1986;23:223-9.
7. Harker LA, Malpass TW, Branson HE, Hessel EA, Slichter SJ. Mechanism of abnormal bleeding in patients undergoing cardiopulmonary bypass: acquired transient platelet dysfunction associated with selective alpha-granule release. Blood 1980;56:824-34.
8. Despotis GJ, Santoro SA, Spitznagel E, Kater KM, Cox JL, Barnes P, Lappas DG. Prospective evaluation and clinical utility of on-site monitoring of coagulation in patients undergoing cardiac operation. J Thorac Cardiovasc Surg 1994;107:271-9.
9. Lemmer JH, Stanford W, Bonney SL, et al. Aprotinin for coronary bypass operations: efficacy, safety, and influence on early saphenous vein graft

patency. A multicenter, randomized, double-blind, placebo-controlled study. J Thorac Cardiovasc Surg 1994;107:543-51.

10. Tatar H, Çiçek S, Demirkiliç U, et al. Topical use of aprotinin in open heart operations. Ann Thorac Surg 1993;55:659-61.
11. De Bonis M, Cavaliere F, Alessandrini F, et al. Topical use of tranexamic acid in coronary artery bypass operations: a double-blind, prospective, randomized, placebo-controlled study. J Thorac Cardiovasc Surg 2000;119:575-80.
12. Rocha E, Hidalgo F, Llorens R, Melero JM, Arroyo JL, Páramo JA. Randomized study of aprotinin and DDAVP to reduce postoperative bleeding after cardiopulmonary bypass surgery. Circulation 1994;90:921-7.
13. Daily PO, Lamphere JA, Dembitsky WP, Adamson RM, Dans NF. Effect of prophylactic epsilon-aminocaproic acid on blood loss and transfusion requirements in patients undergoing first-time coronary artery bypass grafting. A randomized, prospective, double-blind study. J Thorac Cardiovasc Surg 1994;108:99-106.
14. Jamieson WR, Dryden PJ, O'Connor JP, Sadeghi H, Ansley DM, Merrick PM. Beneficial effect of both tranexamic acid and aprotinin on blood loss reduction in reoperative valve replacement surgery. Circulation 1997;96(Suppl 9):96-100.
15. Katoh J, Tsuchiya K, Sato W, Nakajima M, Iida Y. Additional postbypass administration of tranexamic acid reduces blood loss after cardiac operations. J Thorac Cardiovasc Surg 1997;113:802-4.
16. Wong BI, McLean RF, Fremes SE, et al. Aprotinin and tranexamic acid for high transfusion risk cardiac surgery. Ann Thorac Surg 2000;69:808-16.
17. Bidstrup BP, Harrison J, Royston D, Taylor KM, Treasure T. Aprotinin therapy in cardiac operations: a report on use in 41 cardiac centers in the United Kingdom. Ann Thorac Surg 1993;55:971-6.
18. Dodsworth H, Dudley HA. Increased efficiency of transfusion practice in routine surgery using pre-operative antibody screening and selective ordering with an abbreviated crossmatch. Br J Surg 1985;72:102-4.
19. Ferraris VA, Brown JR, Despotis GJ, et al. 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg 2011;91:944-82.
20. Myles PS, Smith JA, Forbes A, et al. Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery. N Engl J Med 2017;376:136-48.
21. Casati V, Sandrelli L, Speziali G, Calori G, Grasso MA, Spagnolo S. Hemostatic effects of tranexamic acid in elective thoracic aortic surgery: a prospective, randomized, double-blind, placebo-controlled study. J Thorac Cardiovasc Surg 2002;123:1084-91.
22. Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. BMJ 2012;344:e3054.
23. Fawzy H, Elmistekawy E, Bonneau D, Latter D, Errett L. Can local application of Tranexamic acid reduce post-coronary bypass surgery blood loss? A randomized controlled trial. J Cardiothoracic Surg 2009;4:25.
24. Abul-Azm A, Abdullah KM. Effect of topical tranexamic acid in open heart surgery. Eur J Anaesthesiol 2006;23:380-4.
25. Sharma V, Fan J, Jerath A, et al. Pharmacokinetics of tranexamic acid in patients undergoing cardiac surgery with use of cardiopulmonary bypass. Anaesthesia 2012;67:1242-50.
26. Casati V, Bellotti F, Gerli C, et al. Tranexamic acid administration after cardiac surgery: a prospective, randomized, double-blind, placebo-controlled study. Anesthesiology 2001;94:8-14.
27. Zabeeda D, Medalion B, Sverdlov M, et al. Tranexamic acid reduces bleeding and the need for blood transfusion in primary myocardial revascularization. Ann Thorac Surg 2002;74:733-8.
28. Wąsowicz M, Jerath A, Bojko B, Sharma V, Pawliszyn J, McCluskey S. Use of a novel technique, solid phase microextraction, to measure tranexamic acid in patients undergoing cardiac surgery. Can J Anaesth 2012;59:14-20.
29. Manji RA, Grocott HP, Leake J, et al. Seizures following cardiac surgery: the impact of tranexamic acid and other risk factors. Can J Anaesth 2012;59:6-13.
30. Kalavrouziotis D, Voisine P, Mohammadi S, Dionne S, Dagenais F. High-dose tranexamic acid is an independent predictor of early seizure after cardiopulmonary bypass. Ann Thorac Surg 2012;93:148-54.

Research Article

E Journal of Cardiovascular Medicine

EJCM 2019;7(1):22-27

DOI: 10.32596/ejcm.galenos.2019.00004

Adherence of Rheumatic Heart Disease Patients to Secondary Prophylaxis and Main Reasons for Poor Adherence at Jimma Medical Center

Kenzu Mohammed[1], Wondu Reta Demissie[2], Moyeta Bariso Gare[2]

[1]Jimma University Institute of Health, Faculty of Medicine, Jimma, Ethiopia
[2]Jimma University Institute of Health, Department of Biomedical Sciences, Jimma, Ethiopia

Abstract

Objectives: Rheumatic heart disease (RHD) is the major long-term sequel of acute rheumatic fever (ARF), which involves the cardiac valves leading to stenosis or regurgitation with resultant hemodynamic disturbance. The incidence of ARF and prevalence RHD in the sub-Saharan Africa including Ethiopia are amongst the highest in the world. The main priority of long-term management of ARF or RHD is to ensure that patients are adherent to the secondary prophylaxis which is monthly benzathine penicillin injection to prevent recurrent attacks of ARF.

Materials and Methods: A cross-sectional study was conducted among sampled 241 RHD patients having at least one year follow-up at cardiac clinic of Jimma Medical Center (JMC) who appointed every month to receive injections of antibiotic prophylaxis. The data was collected for 4 months (from June 1-September 30, 2018) by asking their follow-up status of last one year retrospectively and assessing related variables by using face to face interview. After the data was collected using structured questionnaires, it was coded, entered into Epi data and exported to SPSS for further analysis. The adherence rate of RHD patients was determined by frequency of annual injections of prophylaxis.

Results: A total of 241 patients with RHD were interviewed, among those 224 (93.0%) were received the secondary prophylaxis at least once within last one year, despite frequency differs while 17 (7.0%) of them didn't initiate the prophylaxis yet. The adherence rate

Address for Correspondence: Wondu Reta Demissie, Jimma University Institute of Health, Department of Biomedical Sciences, Jimma, Ethiopia
Phone: +251913988722 **e-mail:** majore04@gmail.com **ORCID ID:** orcid.org/0000-0002-9888-0774
Received: 12.02.2019 **Accepted:** 24.02.2019

Cite this article as: Mohammed K, Demissie WR, Bariso M. Adherence of Rheumatic Heart Disease Patients to Secondary Prophylaxis and Main Reasons for Poor Adherence at Jimma Medical Center. EJCM 2019;7(1):22-27. DOI: 10.32596/ejcm.galenos.2019.00004

Abstract

of the assessed RHD patients to secondary prophylaxis was 55.2% while the left 108 RHD patients (44.8%) were generalized as non-adhered to the prophylaxis [can be who either don't start the prophylaxis 17 (7.0%) or who missed the prophylaxis more than three times annually 86 (35.6%)]. The main reasons for poor adherence were lack of money 41 (38%), far distance from hospital 28 (26%), fear of medication side effects and painful injection 25 (23%), and lack of knowledge about the disease and prevention 14 (13%).

Conclusion: RHD patients attending cardiac clinic of JMC had low adherence rate (55.2%) to the secondary prophylaxis due to lack of money, far distance from the setup, painful injection especially among children and lack of awareness about the disease.

Keywords: Rheumatic heart disease patients, adherence, main reasons of poor adherence

Introduction

Acute rheumatic fever (ARF) and rheumatic heart disease (RHD) represent the first cause of cardiac mortality among children and young people in developing countries[1]. The worldwide prevalence of RHD is estimated to 15.6 million people, with an annual incidence of ARF of 470,000. The burden of mortality still concerns 230,000 people per annum, caused by infective endocarditis and heart failures[2,3].

The prevalence of heart diseases in children and young adults, including congenital heart disease and RHD are highest but underestimated due to many reasons[4].

The prevalence of RHD was also highest in Ethiopia as revealed by many studies that conducted in different parts of the country among school children and other groups which needs due emphasis on management protocols[5-10].

Since 1980s, the recommendations of World Health Organization is to promote secondary prevention as the cornerstone of control programs by continuous administration of specific antibiotics to patients with a previous attack of rheumatic fever, or well-documented RHD[11]. Secondary prevention of rheumatic fever has multipurpose, applicable and cost effective strategy to prevent colonization or infection of the upper respiratory tract with group A β-hemolytic streptococcal pharyngotonsillitis and the development of recurrent attacks of rheumatic fever, to reduce mortality and morbidity due to disease[12-16].

The recommended secondary prophylaxis is intramuscular injections of benzathine benzyl penicillin G (BPG), every three to four weeks which is determined by a number of factors, including age, time since the last episode of ARF, ongoing risk of streptococcal infections and potential harm from recurrent ARF and its dosage being adapted to patient's weight[12,17].

The implementation of monthly administration of secondary prophylaxis to all RHD patients should need due emphasis and its effectiveness in reducing rates of streptococcal pharyngitis, recurrences of ARF and the progression of RHD should clearly evaluated periodically; otherwise it might even lead to mild to moderate valvular lesions within a decade[18-20]. Thus simultaneously promoting adherence of patients to secondary prophylaxis should be addressed and assessed timely as the management modality[21]. Patient adherence is defined as the concordance between the patient's behavior and the care provider's recommendations[18,22]. Global adherence to treatment of chronic diseases in developed countries averages only 50%, particularly affecting the poor population[23]. As many factors interact and interfere with adherence, it is considered as a multidimensional phenomenon[24].

Even though the level of adherence required to prevent further episodes of ARF is not known, the objective is to reach 100% of the annual expected BPG injections, with a recommended benchmark of 80%[25]. Patients receiving

less than 80% of prescribed doses are considered as none adhered with high risk of recurrence of ARF[15,25].

The objective of the present study was to evaluate rates of adherence of RHD patients attending cardiac clinic of Jimma Medical Center (JMC) to BPG injection prophylaxis and to assess the reasons for poor adherence.

Materials and Methods

Study Design and Setting

The cross sectional study was conducted among RHD patients attending Cardiac Clinic of JMC for at least one year who appointed every month to receive secondary prophylaxis. JMC is located in Jimma zone, Southwest Ethiopia which is the largest and pioneer referral specialized teaching hospital of the country, serving millions of patients dwelling in the catchment area. The study was conducted for 4 months (from June 1-September 30, 2018 among RHD patients). Information of pediatrics was received from their corresponding parents or caregivers.

Data Collection Technique Processing and Analysis

Standardized and structured questionnaire was used for data collection. The collected data was cleaned, coded, entered in to Epi data version 3.1 and finally exported to SPSS version 22 for further analysis. Adherence of RHD patients was determined based on frequency of annual prophylaxis they received and considered as adhered, not adhered and not started the prophylaxis yet. For pediatric RHD patients, their family's adherence (bringing child to the institution for receiving prophylaxis was evaluated).

Ethical Considerations

Approval of the proposal was obtained from Institutional Review Board of Jimma University, Institute of Health (IRB/989/2018). An informed written consent was obtained from patients or/and parents of pediatric patients less than 16 years after explaining the purpose of the study. The respondents were also informed that the obtained information would not be disclosed to a third party.

Operational Definition

Good adherence or adhered to prophylaxis: if the rate of adherence was covering ≥80% of prophylaxis (patient was not missed any injection or only missed three or less than three times injection in the last 1 year or received prophylaxis nine or more than nine times).

Poor adherence or not adhered to prophylaxis: if the rate of adherence is <80% (patient had missed their regular injection more three times in the last 1year).

Results

Socio-demographic Characteristics

During the period of June 1-September 30, 2018, a sample of 241 RHD patients who came to Cardiac Clinic of JMC for follow-up were interviewed, of these 135 (56%) were pediatric age group (age 5-16 years) and 106 (44%) were adult age group as the overall age ranges from 5-68 years. The male to female ratio was 1:1.2 computed from 135 (56.0%) females and 106 (44.0%) males. Majority of the patients were dwelling in rural part 172 (71.4%) while urban dwellers account 69 (28.6%). Majority of RHD patients were illiterate [90 (37.3%)] while 36 (14.9%) and 62 (25.7%) attended grade 5-8 and grade 9-12 respectively. Majority of the patients or their care givers were farmers 151 (62.7%) who were considered as low income with monthly income below 1000 Ethiopian birr (53.9%). Majority of the patients [195 (80.9%)] were living at the distance of more than 3 kilometers away from JMC where they seek service. The detail is well seen in Table 1.

Adherence Status of RHD Patients to Secondary Prophylaxis

Out of a total of 241 patients, majority of them 224 (93.0%) took secondary prophylaxis (intra muscular injection of BPG) during follow-up of last one year despite frequency varies. From a total of 224 RHD patients who took secondary prophylaxis, 86 (35.6%) of them missed their regular injection for more than three times and 5 (2.1%) never missed any annual prophylaxis (100% coverage) last year who have to be appreciated. In

general the adherence rate of RHD patients to secondary prophylaxis was 133 (55.2%) who received more than nine annual prophylaxis or missing less than three months while the left 108 (44.8%) considered non adhered [can be either who don't start prophylaxis yet (7.0%) or who missed more than three times of last year prophylaxis (35.6%)] as detailed in Table 2.

Table 1. Socio-demographic characteristics of rheumatic heart disease patients at Jimma Medical Center Cardiac Clinic, Jimma, Ethiopia, 2018

Socio-demographic		Number/ frequency	Percentage (%)
Sex	Male	106	44
	Female	135	56
Age	<16 years	135	56
	>16 years	106	44
Religion	Muslim	163	67.6
	Orthodox	52	21.6
	Protestant	19	7.9
	Others	7	2.9
Ethnicity	Oromo	165	68.5
	Amahara	44	18.3
	Dawaro	16	6.6
	Tigre	4	1.7
	Gurage	5	2.1
	Others	7	2.9
Family income	<1000 Ethiopian birr	230	53.9
	>1000 Ethiopian birr	111	46.1
Educational status of (patient/care taker)	Illiterate	90	37.3
	Read and write only	24	10
	Grade 1-4	14	5.8
	Grade 5-8	36	14.9
	Grade 9-12	62	25.7
	Higher	15	6.2
Occupation	Farmer	151	62.7
	Government employee	27	11.2
	Merchant	35	14.5
	Daily labor	23	9.5
	Others	5	2.1
Address	Urban	69	28.6
	Rural	172	71.4

Reasons for Poor Adherence

The main reasons to miss and don't initiate their prophylaxis among the 108 RHD patients with poor adherence were lack of money 41 (38%), followed by far distance from hospital 28 (26%), fear of medication side effects and painful injection 25 (23%), and lack of knowledge about the disease and prevention 14 (13%).

Discussion

Among the total 241 RHD patients assessed, majority of them (56%) were pediatric age group (age 5-16 years) and female (56%) dwelling in rural part (71.4%) which is also in line with global epidemiology of the disease being highest among school children, females and rural part[3,5].

The level of adherence of RHD patients to secondary prophylaxis was 55.2% as computed from the annual frequency of intramuscular injection (more than 9 times per last year is considered as adhered) which was very low and needs due emphasis. This low adherence rate is also in harmony with the study of Musoke et al. who reported the adherence rate of 54%, also in nearly similar range with the finding of systematic analysis done by Kevat et al. and Amarilyo et al.[26-28].

But the present finding was against the studies of de Dassel et al. with their finding of high adherence rate of 63.5-67.5% probably due to study design difference as they approach by register data analysis, the finding of Nicola Culliford-Semmens et al. who revealed maximum adherence rate of RHD patients to secondary prophylaxis

Table 2. Adherence status of rheumatic heart disease patients to secondary prophylaxis, Jimma, Ethiopia, 2018

Status of adherence	Number/ frequency	Percentage (%)
Not initiated yet	17	7.0
Received prophylaxis 12 times annually (not missed any)	224 5	93.0 2.1
>9 times annually (missed <3 times)	133	55.2
<9 times annually (missed >3 times)	86	35.6
Adherence status: adhered to prophylaxis (missed <3 times)	133	55.2
Not adhered to prophylaxis (not start yet + missed >3 times)	108	44.8

(92%) due to the socio-demographic difference of our patients and New Zealand and design difference[29,30]. Opposing the finding of the present study, highest adherence of RHD patients to secondary prophylaxis was also reported by studies of Sial et al. (73.5%), Saxena et al. (93.6%) may be due to study design and socio-demographic difference[31,32].

The finding of present study was also inconsistent with the study of Gasse et al. and Pelajo et al. who reported even lower adherence rate (46%) and (32-42%)[33,34]. The probable justification for this difference is a significant variation in study design and socio-demographic characteristics.

The main reasons/barriers affecting low adherence rate of RHD patients to secondary prophylaxis was lack of money, far distance to the setting, painful injection and lack of awareness about the disease. This objective was also in line with the study of Petricca et al. who conducted at the setting to explore those barriers (disease perception, quality of service and cost)[35]. The present finding for reasons of low adherence was also supported with study of Musoke et al. that conducted in Uganda and Nemani who explored the absence of proper counseling followed by a sense of well-being, injection site pain and financial constraints as the main reasons for low adherence[26,36].

Acknowledgements

I would like to thank Jimma University and Community Based Education Office for providing this golden opportunity and stationery provision. I would also like to thank JMC for permission of data collection. At last but not least, my honored thanks go to data collectors (cardiac clinic staff nurses) and RHD patients and pediatric correspondents for their invaluable cooperation for the success of the study.

Ethics

Ethics Committee Approval: Institutional Review Board (IRB/989/2018 of Jimma University, Institute of Health).

Informed Consent: An informed written consent was obtained from patients or/and parents of pediatric patients less than 16 years after explaining the purpose of the study. The respondents were also informed that the obtained information would not be disclosed to a third party.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.M., W.R.D., M.B.G., Concept: K.M., W.R.D., M.B.G., Design: K.M., W.R.D., Data Collection or Processing: K.M., Analysis or Interpretation: K.M., W.R.D., Literature Search: K.M., W.R.D., Writing: K.M., W.R.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. Lancet 2012;379:953-964.
2. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. Lancet Infect Dis 2005;5:685-94.
3. Seckeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clin Epidemiol 2011 Feb 22;3:67-84.
4. Zühlke L, Mirabel M, Marijon E. Congenital heart disease and rheumatic heart disease in Africa: recent advances and current priorities. Heart 2013;99:1554-61.
5. Gemechu T, Mahmoud H, Parry EH, Phillips DI, Yacoub MH. Community-based prevalence study of rheumatic heart disease in rural Ethiopia. Eur J Prev Cardiol 2017;24:717-723.
6. Günther G, Asmera J, Parry E. Death from rheumatic heart disease in rural Ethiopia. Lancet 2006;367:391.
7. Befekadu H, Shehab A, Mocumbi AO, Aguib Y, Yacoub MH. Genetic susceptibility to rheumatic heart disease in three African populations: Egypt, Ethiopia and Mozambique. Curr Trend Cardiol 2017;1.
8. Mulatu HA, Woldemichael M, Aberra M. Prevalence of Rheumatic Heart Disease among Primary School Students in Mid-Eastern Ethiopia. Biol Syst Open Access 2015 Dec 26;5:1-4.
9. Yadeta D, Hailu A, Haileamlak A, et al. Prevalence of rheumatic heart disease among school children in Ethiopia: A multisite echocardiography-based screening. Int J Cardiol 2016;221:260-3.
10. Professor David Phillips-Honorary Advisor-THET. Rheumatic heart disease: a forgotten killer in low-income countries. THET 2017. Available

from: https://www.thet.org/rheumatic-heart-disease-forgotten-killer-low-income-countries/

11. World health organization. WHO programme for the prevention of rheumatic fever/rheumatic heart disease in 16 developing countries: report from Phase I (1986-90). WHO Cardiovascular Diseases Unit and principal investigators. Bull World Health Organ 1992;70:213-18.
12. Manyemba J, Mayosi BM. Intramuscular penicillin is more effective than oral penicillin in secondary prevention of rheumatic fever--a systematic review. S Afr Med J 2003;93:212-8.
13. WHO Study Group on Rheumatic Fever and Rheumatic Heart Disease ([2001: Geneva, Switzerland])" & World Health Organization. ([2004])". Rheumatic fever and rheumatic heart disease: report of a WHO expert consultation, Geneva, 20 October-1 November 2001. Geneva: World Health Organization. http://www.who.int/iris/handle/10665/42898
14. Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. Circulation 2009;119:1541-51
15. RHD Australia (ARF/RHD writing group) National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: The Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. 2nd edition. RHD Australia: Menzies School of Health Research; 2012.
16. Steer AC, Colquhoun S, Kado J, Carapetis JR. Secondary prophylaxis is important for the prevention of recurrent rheumatic fever in the Pacific. Pediatr Cardiol 2011;32:864-5.
17. Manyemba J, Mayosi BM. Penicillin for secondary prevention of rheumatic fever. Cochrane Database Syst Rev 2002, CD002227.
18. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database Syst Rev 2008, CD000011.
19. Steer AC, Carapetis JR. Prevention and treatment of rheumatic heart disease in the developing world. Nat Rev Cardiol 2009;6:689-98.
20. Alex B, Warren W. Diagnosis and management of acute rheumatic fever and rheumatic heart disease in Australia, National heart foundation of Australia; 2012;590:1-100.
21. Engelman D, Mataika RL, Kado JH, et al. Adherence to secondary antibiotic prophylaxis for patients with rheumatic heart disease diagnosed through screening in Fiji. Trop Med Int Health 2016;21:1583-91.
22. Osterberg L, Blaschke T: Adherence to medication. N Engl J Med 2005;353:487-97.
23. Global adherence to treatment of chronic diseases in developed countries averages only 50%, particularly affecting the poor population.
24. World Health Organisation: Adherence to long-term therapies. Evidence for action. Geneva, Switzerland: World Health Organization; 2003. Gasse et al. BMC Public Health 2013, 13:131 Page 8 of 9 http://www.biomedcentral.com/1471-2458/13/131
25. World Heart Federation: Diagnosis and Management of Acute Rheumatic Fever Rheumatic Heart Disease. Geneva: World Heart Federation before; 2007.
26. Musoke C, Mondo CK, Okello E, et al. Benzathine penicillin adherence for secondary prophylaxis among patients affected with rheumatic heart disease attending Mulago Hospital. Cardiovasc J Afr 2013;24:124-9.
27. Kevat PM, Reeves BM, Ruben AR, Gunnarsson R. Adherence to Secondary Prophylaxis for Acute Rheumatic Fever and Rheumatic Heart Disease: A Systematic Review. Curr Cardiol Rev 2017;13:155-166
28. Amarilyo G, Chodick G, Zalcman J, et al. Poor long-term adherence to secondary penicillin prophylaxis in children with history of rheumatic fever. Semin Arthritis Rheum 2018 Oct 16.
29. Dassel JL de, Fittock MT, Wilks SC, Poole JE, Carapetis JR, Ralph AP. Adherence to secondary prophylaxis for rheumatic heart disease is underestimated by register data. PLoS One 2017, e0178264.
30. Culliford-Semmens N, Tilton E, Webb R, et al. Adequate adherence to benzathine penicillin secondary prophylaxis following the diagnosis of rheumatic heart disease by echocardiographic screening. N Z Med J 2017;130:50-57.
31. Sial JA, Farman MT, Batra MK, Karim M. Adherence to secondary prophylaxis of rheumatic fever in patients with rheumatic heart disease in rural areas. Pak Heart J 2018;51:243-47.
32. Saxena A, Mehta A, Ramakrishnan S. Adherence to Benzathine Penicillin in Children with Rheumatic Fever/Rheumatic Heart Disease: Results from an Indian Pediatric Rhd Registry. J Am Coll Cardiol 2015;65.
33. Gasse B, Baroux N, Rouchon B, Meunier JM, Frémicourt ID, D'Ortenzio E. Determinants of poor adherence to secondary antibiotic prophylaxis for rheumatic fever recurrence on Lifou, New Caledonia: a retrospective cohort study. BMC Public Health 2013;13:131.
34. Pelajo CF, Lopez-Benitez JM, Torres JM, de Oliveira SK. Adherence to secondary prophylaxis and disease recurrence in 536 Brazilian children with rheumatic fever. Pediatr Rheumatol Online J 2010;8:22.
35. Petricca K, Mamo Y, Haileamlak A, Seid E, Parry E. Barriers To effective follow-up treatment for rheumatic heart disease in Jimma, Ethiopia: A grounded theory analysis of the patient experience. Ethiop J Health Sci 2009;19:39-44.
36. Nemani L, Maddury J, Barik R, Arigondam AK. A Cross-sectional study to look at the determinants of poor adherence to secondary penicillin prophylaxis for rheumatic heart disease at a tertiary care center in South India. J Clinical and Preventive Cardiology 2018;7:5-10.

Research Article

E Journal of Cardiovascular Medicine

EJCM 2019;7(1):28-35

DOI: 10.32596/ejcm.galenos.2019.00013

Extra-corporeal Membrane Oxygenation Procedures on YouTube: What Practices Have Being Show

Tuğra Gençpınar[1], Çağatay Bilen[2], Serdar Bayrak[1], Gökmen Akkaya[2], Volkan Hancı[3], Sibel Büyükçoban[3]

[1]Dokuz Eylül University Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Turkey
[2]Ege University Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Turkey
[3]Dokuz Eylül University Faculty of Medicine, Department of Anesthesiology and Reanimation, İzmir, Turkey

Abstract

Objectives: To the our best knowledge, there is no literature on the effectiveness of YouTube on extra-corporeal membrane oxygenation (ECMO) practice. In our study, we aimed to evaluate the characteristics and medical aspects of videos on YouTube about ECMO.

Materials and Methods: In internet media website YouTube.com search engine; the word ECMO was searched in December 2018 without any filter. The listed first 100 videos were classified according to count of like, dislike, origin of country and types of ECMO. ECMO videos were categorized under three main topics as, educational purpose, patient follow-up and weaning from ECMO. The materials were evaluated in terms of intelligibility using the suitability assessment of materials (SAM). User participation measurements were obtained for each video.

Results: In our study, it was observed that the number of videos, content variety and duration of ECMO contents that were uploaded to YouTube after 2016 increased significantly. However, it was found that there was no significant relationship between date and duration of SAM and there was no significant correlation between the duration of the video and the SAM score. However, it was determined that there was a positively weak correlation between the scores of the videos and the number of views.

Conclusion: Medical education is forming from didactic education to a system which is problem-based, media and visually aided, and effectively using all of the educational tools. During this period, the use of sites such as YouTube is increasing among medical education sources. Considering that, the discussions may be based on insufficient information quality, patient confidentiality and legal issues. Thus, we think that the necessity of double-blind peer

Address for Correspondence: Tuğra Gençpınar, Dokuz Eylül University Faculty of Medicine, Department of Cardiovascular Surgery, İzmir, Turkey
e-mail: tugra01@yahoo.com **ORCID ID:** orcid.org/0000-0003-4438-7991
Received: 06.03.2019 **Accepted:** 13.03.2019

Cite this article as: Gençpınar T, Bilen Ç, Bayrak S, Akkaya G, Hancı V, Büyükçoban S. Extra-corporeal Membrane Oxygenation Procedures on YouTube: What Practices Have Being Show. EJCM 2019;7(1):28-35.
DOI: 10.32596/ejcm.galenos.2019.00013

reviews is one of the important points to discuss in terms of content, educational direction, patient confidentiality and legal procedures in social media related to medical education.

Keywords: Medical knowledge, e-learning, YouTube, femoral arter, ECMO, cardiovascular surgery, web-based learning

Introduction

With the development of the internet, as in all other disciplines, the speed of information exchange and the use of communication media have increased considerably in the health services sector. In the active medical education system, students are encouraged to have access to current online publications and visual aids[1]. YouTube video sharing is one of the most frequently used one in social media for educational purpose. Raikos and Waidyasekara found that shared 294 videos were involving beneficial scientific data for medical students on the YouTube about the surgical anatomy of the heart[2]. The researchers stated that these can contribute to clinical branches by sharing more.

Medical educators, students, practitioners, physicians, auxiliary health personnel, and even patients often follow YouTube's relevant visual documents and videos on the website in order to visually learn and interpret medical conditions. YouTube is a video hosting website, locates in San Bruno, California, United States of America[1,2]. Approximately, 100 videos have being added by users worldwide in every minute[1]. However, these videos cannot be verified and are submitted by non-peer-reviewed sources. As a result, such studies analyzing YouTube's educational content have been reporting limited results. Moreover, these studies were not able to exclude non-educational videos from unreliable sources. On the other hand, several articles declare that YouTube videos which have been prepared with reliable sources and suitable for educating the public have a high educational value. Reliable videos on cardiovascular diseases are watched in terms of compliance with treatment, screening, or prevention[1-6]. Since 2007, various results on YouTube's educational content have been reported[1-9]. As a consequence of these varied findings, researches involving medical YouTube videos decreased by 83% in one year[9-11]. Desai et al. have evaluated 139 YouTube videos for global laparoscopic techniques for cholecystectomy, therefore, suggested some YouTube videos for surgical techniques[11]. Furthermore, thereby considering the Spearman correlation coefficient (SCC) for the development of surgical applications, they have concluded that the technological infrastructure provides convenience in surgical practice. The value of SCCs is feasible in grading and assessing about visual video quality and utility.

Extra-corporeal membrane oxygenation (ECMO) is one of the most important and widely used medical device that provides lung or heart circulation support in reversible conditions of cardiac or respiratory failure, therewithal mostly utilized in case of failure to weaning from the cardiopulmonary by-pass (CPB)[11-13]. ECMO may be implanted in order to bridging for long-term ventricular assist device in cardiomyopathies or in case of cardiac arrest due to any reason, and patients where the patient is unstable or unresponsive to the cardiopulmonary resuscitation (CPR). Nonetheless, in high-risk catheter interventions, the ECMO can be fitted as an elective support either. However, the issue of which type of ECMO should be installed is also important. For instance, in case of ischemic cardiogenic shock or when the patient failed to wean from CPB after cardiac surgery, veno-arterial ECMO support is preferred. On the other hand, veno-venous ECMO is frequently chosen in patients with reversible lung pathologies.

Recent articles regarding ECMO's indications, follow-up, complications, positive contribution to transplantation are frequently studied in the literature. The aim of this

study is to review the ECMO videos in YouTube and to discuss them with literature.

Materials and Methods

Between the dates of 1-30 December 2018, by searching the keyword "ECMO" in YouTube search, we have determined the videos with medical content. Then we listed the first 100 videos focused on the cardiac, vascular or cardiovascular fields. The number of likes-dislikes, country origins of the videos which were related to ECMO treatment had been investigated. In terms of the number of views, likes, and comments, the evaluation of intelligibility was performed by using the suitability assessment of materials (SAM) by examining the videos for medical education[11]. User participation measurements were reviewed for each video. Most of the videos were involving the subjects of ECMO's functioning, implementation or had a feature of being educational videos. In assessment, researchers focused on the type, duration and history of ECMO video content. Due to there is no verified scoring system available for the videos yet; the video contents was categorized according to 7 different educational contents as; 1) ECMO initiation, 2) ECMO monitoring, 3) ECMO termination, 4) ECMO indications, 5) ECMO complications, 6) treatment/management and, 7) preventing ECMO complications. Our study has also adopted this quantitative method in data collection and analysis. Moreover, we developed a research method basing on behavioral appreciation and follow-up rates[11].

Our study is based on a web research therefore ethical approval did not obtained and does not include any patient, for this reason there was no need to obtain an informed consent form.

Evaluating the Eligibility of Videos

SAM evaluated the videos by using variables as; 1) content of the videos, 2) level of informativeness, 3) graphics, 4) order and typography, 5) learning stimulation and, 6) cultural fitness variables then a separate SAM score was calculated for each video[11].

Following a rating of 100 over SAM, videos with 0-39 cumulative raw score was identified as "insufficient", 40-69 cumulative raw score was accepted as "sufficient" and 70-100 cumulative raw scores were considered as "superior".

Evaluating the User Engagement

Five user interaction measurements recorded for each video; 1) views, 2) likes, 3) dislikes, 4) favorites and, 5) comments. These data were collected between the dates of 1-30 December 2018.

Statistical Analysis

Acquired data was analyzed using a SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) 20.0 software. Kruskal-Wallis and Mann-Whitney U tests were used to compare the groups. A p value less than 0.05 was considered as significant difference.

Results

In our study, the listed first 100 videos following a search with ECMO keyword in the YouTube search engine between the dates of 1-30 December 2018 were evaluated. Overall 13 hours 20 minutes and 38 seconds of footage were examined. The longest video was 1 hour 54 minutes and 46 seconds, meanwhile the shortest one was 28 seconds. The most liked video had 223 likes while the least one had none. Nonetheless, the most viewed video was viewed for 117.955 times, this number was minimum 32 for the least. The number of comments for videos was varying between 0 and 223. The average number of views was 14956.14±22044.00, while the average number of "likes" was 33.33±48.29; the mean number of "dislike" was found to be 2.44±4.05 and the mean video duration was observed as 13.11±17.32 minutes.

Twelve (12%) of the videos were containing animation. Seventeen (17%) of the videos provide information on cannulation and 8 (8%) of them on decannulation. There withal, 37 (37%) of the videos were about ECMO indications, 36 (36%) were about ECMO complications. On the other hand, 33 (33%) of all videos were mentioning treatment and management of complications, and 31 (31%) of them were related to prevention of complications.

Eighteen (18%) of the videos were containing a footage from operating room. Fifty six (56%) videos were containing information about veno-arterial ECMO, while 48 (48%) video were involving information about veno-venous ECMO. While 61 (61%) of the videos were for educational purposes, 56 (56%) videos were simply explaining the operation principle of ECMO. Twenty three (23%) videos were including radiological examinations that used during cannulation, follow-up or complications. The videos were evaluated according to SAM score. The highest score was 36 (95%) and the lowest one was calculated as 3 (8%). When the videos had evaluated via SAM score, 21 videos were in the insufficient group and 49 were in sufficient group. Besides, 30 videos were found in superior group.

There was no significant correlation between the duration of the video and the SAM score ($p>0.05$). A positive correlation was found between the SAM score of the videos and the number of views ($p=0.046$; $r=0.200$). Similarly, there was a positive correlation between the percentage of SAM and the number of views ($p=0.042$; $r=0.204$). However, there was no detected significant correlation between SAM score and number of likes, dislike, and comments. There was a positive correlation between the number of views and number of likes ($p<0.001$; $r=0.689$), dislikes ($p<0.001$; $r=0.663$) and comments ($p<0.001$; $r=0.645$). Moreover, no significant difference was found between the SAM groups and the origin of countries ($p=0.725$).

When the videos are reviewed by uploading years, 4% was loaded into YouTube before 2010, while 36% were between years 2011-2015 and 60% were after 2016. This finding may be interpreted as that the use of YouTube as a source of information concerning ECMO is increasing recently (Table 1: video content distribution)[1-3]. According to SAM groups and within advancing years, video contents and characteristics demonstrated statistically significant changes (Table 2: video characteristics according to years and SAM groups), [Table 3: comparison of the content of

Table 1. Video content distribution

Video content	+ (%)	- (%)	Total (%)
Animation	12	88	100
Cannula procedure	17	83	100
ECMO monitoring	32	68	100
Decannulation	8	92	100
Indication	37	63	100
Complication	36	64	100
Treatment management	33	67	100
Complication prevention	31	69	100
Operating room image	18	82	100
Venoarteriel	56	44	100
Venovenous	48	52	100
Working principle	56	44	100
Radiological examination	23	77	100
Educative	61	39	100
HD image	64	36	100

ECMO: Extra-corporeal membrane oxygenation, HD: High-definition

Table 2. Video characteristics according to years and suitability assessment of materials groups (mean ± standard deviation)

Years	Follow-up	Like	Dislike	Comment	Time
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
2010 and earlier (n=4)	22213.75±14961.07	13.50±17.59	2.25±3.86	7.00±3.46	2.50±1.91
2011-2015 (n=36)	26283.80±29114.14	43.86±51.83	3.19±3.70	4.00±5.44	8.02±9.01
2016 and later (n=60)	7675.70±12860.9	28.33±46.71	1.25±2.58	1.21±2.16	16.86±20.42
p	**<0.001**	**0.063**	**0.005**	**<0.001**	**0.018**
SAM group					
Insufficient (n=21)	13055.23±15204.59	23.42±30.30	2.76±3.52	2.66±3.73	6.80±9.81
Sufficient (n=49)	8018.26±13344.69	27.34±44.03	1.02±2.05	1.27±2.42	18.67±20.72
Superior (n=30)	27618.63±30901.27	50.03±60.79	3.03±3.99	4.33±5.69	8.43±11.96
p	**0.002**	**0.632**	**0.040**	**0.015**	**0.02**

SAM: Suitability assessment of material, SD: Standard deviation

videos over the years[1-3]], (Table 4: number of videos per year).

The top three countries which had been the most ECMO video source were the USA, India and England. Only 64 (64%) of the videos had high-definition (HD) image quality and this rate had significantly increased after 2015 (p<0.001). Number of views, likes, dislikes, comments, video lengths, overall and percentage of SAM scores were not statistically different in comparisons when the videos were classified according to country origin and presence/absence of HD quality (p>0.05).

Discussion

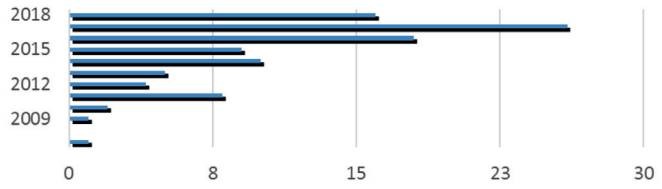
In this study, the relevance, content, and user engagement of the videos on YouTube about ECMO were evaluated.

Table 3. Comparison of the content of videos over the years

Video content/years		≤2010, n (%)	2011-2015, n (%)	≥2016, n (%)	p
Animation	+	0 (0%)	4 (11.1%)	8 (13.3%)	0. 714
	-	4 (100%)	32 (88.9%)	52 (86.7%)	
Cannula procedure	+	0 (0%)	7 (19.4%)	10 (16.7%)	614
	-	4 (100%)	29 (80.6%)	50 (83.3%)	
ECMO monitoring	+	0 (0%)	6 (16.7%)	26 (43.3%)	**9**
	-	4 (100%)	30 (83.3%)	34 (56.7%)	
Decannulation	+	0 (0%)	2 (5.6%)	6 (10%)	617
	-	4 (100%)	34 (94.4%)	54 (90%)	
Indication	+	0 (0%)	7 (19.4%)	30 (50%)	**3**
	-	4 (100%)	29 (80.6%)	30 (50%)	
Complication	+	0 (0%)	8 (22.2%)	28 (46.7%)	**17**
	-	4 (100%)	28 (77.8%)	32 (53.3%)	
Treatment management	+	0 (0%)	6 (16.7%)	27 (45%)	**6**
	-	4 (100%)	30 (83.3%)	33 (55%)	
Complication prevention	+	0 (0%)	7 (19.4%)	24 (40%)	**42**
	-	4 (100%)	29 (80.6%)	36 (60%)	
Operating room image	+	1 (25%)	6 (16.7%)	11 (18.3%)	914
	-	3 (75%)	30 (83.3%)	49 (81.7%)	
Venoarteriel	+	0 (0%)	15 (41.7%)	41 (68.3%)	**3**
	-	4 (100%)	21 (58.3%)	19 (31.7%)	
Venovenous	+	0 (0%)	13 (36.1%)	35 (58.3%)	**16**
	-	4 (100%)	23 (63.9%)	25 (41.7%)	
Working principle	+	1 (25%)	14 (38.9%)	41 (68.3%)	**8**
	-	3 (75%)	22 (61.1%)	19 (31.7%)	
Radiological examination	+	0 (0%)	5 (13.9%)	18 (30%)	**103**
	-	4 (100%)	31 (86.1%)	42 (70%)	
Educative	+	0 (0%)	17 (47.2%)	44 (73.3%)	**2**
		4 (100%)	19 (52.8%)	16 (26.7%)	
HD image	+	1 (25%)	14 (38.9%)	49 (81.7%)	**>0.001**
	-	3 (75%)	22 (61.1%)	11 (18.3%)	
SAM	Insufficient	3 (75%)	8 (22.2%)	10 (16.7%)	**3**
	Sufficient	0 (0%)	12 (33.3%)	37 (61.7%)	
	Superior	1 (25%)	16 (44.4%)	13 (21.7%)	

ECMO: Extra-corporeal membrane oxygenation, HD: High-definition, SAM: Suitability assessment of material

Table 4. Number of videos per year



The number, content, diversity and duration of videos regarding ECMO which were uploaded YouTube increased significantly after 2016, however, there was no significant relationship between history and SAM score, however, there was no significant relationship between loading date and SAM score. Moreover, there is no significant correlation between the duration of video and SAM score. On the other hand, there was a positively weak correlation between the scores of the videos and the number of views.

While YouTube's content creators have designed it for entertainment rather than education, users share a large number of videos about medical issues that are related to themselves or for medical educational purposes. Without a standardized peer review process or a method where reliable sources can be identified, video searches on YouTube result in a vague mix of video and entertainment-oriented videos. The aim of this study was to evaluate the medical benefits of YouTube by evaluating ECMO videos and presenting them to the literature. We are opinion that such findings may contribute to the visual learning curve by examining what applications are shown about ECMO procedures on YouTube.

Nowadays, educational videos are now being frequently uploaded to the internet via social media sources in the cardiovascular field. When current articles reviewed in the literature concerning this issue, they emphasize that such videos benefit patient management and decision of methods to apply. For instance, Pitcher et al. reviewed common femoral artery interventions in YouTube and other online resources[3]. Although used by medical students, vascular experts are not sufficiently standardized to a basic vascular procedure for access to the femoral artery. However, there is no consensus about femoral interventions or established a certain vascular procedure.

The researchers who are well-known vascular specialists, emphasized that, vascular surgeons should improve the visibility of educational videos in online learning resources. Pandey et al. analyzed the results of Google search, YouTube videos, Twitter messages about left ventricular assist device-heart transplantation then they determined that numbers of studies, searches and upload have been significantly increased during last 7 years on the social media[4]. Similarly in our study, the increase in the number of videos in 2016 and beyond is remarkable. Compatible with this, an increase in the number of videos in 2016 and beyond was observed in our study as well.

Chen et al. implied the importance of YouTube videos in the education process in their study[5]. Furthermore, they stated that uploading more videos concerning heart transplantation with a HD would be better for this purpose. In our study, it was determined that the number of HD videos increased after 2015 in parallel with technological advances.

However, the characteristics of the video, such as number of view, like, dislike, comment, duration, SAM total score and percentages of SAM are not different in comparisons by being videos HD or not. Therefore, these outcomes are interpreted in favor of the quality of the image, content and audiences' responses are not increasing in parallel.

Agrawal et al. have addressed the need for care of in children with congenital coronary anomalies by conducting social media search[6]. On the other hand, Panhuyzen-Goedkoop et al. have evaluated the YouTube videos including sudden athlete deaths in order to evaluate the relation between facial expressions and type of syncope[7]. They pointed out the deficiencies in CPR onset and highlighted the waste of valuable time since the beginning of syncope.

Bademci et al. evaluated the YouTube videos regarding deep venous thrombus[8]. They determined that the videos which were uploaded by clinicians were more educational

thus they suggested that more treatment-diagnostic based videos with animation should be loaded. Moreover, Gunes et al. remarked the importance of public information about varicose veins after evaluating social media videos considering the prevalence of disease[9].

Azer et al. reported the lack of sufficient number of original educational video about the cardiovascular and respiratory system after they reviewed 1920 physical examination and training videos on YouTube[10]. Similarly, Desai et al. analyzed a total of 607 medical content videos on YouTube[11]. In this study, all videos were evaluated in terms of intelligibility using SAM and user participation measurements were obtained for each video. The researchers found that only 27% of the videos they analyzed had superior SAM score. This rate was 30% in our study.

Although the researchers emphasized that the videos with high SAM scores were more educational, they stated that they could not find a significant relationship between high SAM scores and user-based variables such as numbers of view, like, and comment. As a result, they declared that the concept of "content is king" is yet unclear whether it applies to medical videos uploaded by reliable sources for patient education on YouTube[11]. Compatible with this, we used the SAM score and determined that there was a positively weak correlation between the scores of the videos and the number of views. However, a significant correlation between SAM score and user participation parameters, numbers of like, dislike, comment was not determined in our study as well. Interestingly, we found that when videos classified in account of SAM score as insufficient, sufficient and superior, sufficient ones had less view number than insufficient ones. Nonetheless, both sufficient and insufficient groups had similar number of like. This evidence supports that content of video is not always parallel to user engagement assessments therefore the underlying reasons need to be investigated by further studies.

Chen et al. revealed a positive correlation between use of ECMO and the popular ECMO news on social media[12]. As a consequence, they concluded that social media is supportive for public knowledge about ECMO.

Over the last decade, social media has emerged as a new platform for information exchange and interpersonal communication for health professionals[13]. This progress in technology should be used to achieve better clinical results and to share information. However, the basic behaviors of health professionals and the increase of productivity of social media and their ethical use for a sustainable health system remain unclear. Inadequate information quality, patient confidentiality and legal issues are risks and challenges that can affect the effective and useful integration of online platforms. In this respect, our study aimed to clarify the factors related to the frequency of social media usage and user participation on YouTube videos regarding ECMO in the discipline of cardiovascular surgery. Thus we targeted to enhance the communication and collaboration among the health professionals. Consequently, such findings may benefit to get a better knowledge about the behavior of health professionals in their daily practices. To summarize, YouTube is being increasingly used as a platform for to share health information[14].

Our research shows important results regarding the adoption of YouTube in healthcare practice. Based on the findings of this study, we determined that the use of YouTube video eases the information exchange especially among young people and increases the share of medical experiences that support ECMO's learning and development. Moreover, social media platforms contribute to develop a higher level of communication among practitioners and increase daily productivity. In this respect, health services can benefit from interactive platforms. We believe that YouTube video sharing and their awareness are useful in terms of process quality for to develop a vital application such as ECMO. The advancement of online technologies will promote practitioners in collecting, managing and interacting for better quality of service. YouTube increases the exchange of information between healthcare professionals about the optimal decision making process for ECMO initiation.

YouTube's viral marketing potential may to change patients' beliefs about controversial medical issues[15]. A non-expert user is more likely to find such content, and getting related videos depends on the search term used. In addition, healthcare seekers seem to be affected by the language styles of providers depending on web-based communication content[16]. YouTube is being used as a tool to promote non-scientific treatments and medicines that have not yet been approved by appropriate institutions[17]. The importance of video sharing, which has reached more than 90% of global internet traffic by 2020, is supported by a few estimates.

In our study, it has been found that the number, content, diversity of videos about ECMO have increased significantly in recent years. However, there was no significant relationship between upload date and content scores besides there was a positively weak correlation between the content score and the number of views.

In this respect, considering that the discussions in the future may be due to insufficient information quality, patient confidentiality and legal issues, we are in opinion that the necessity of double blind peer review process for social media shares will be one of the most important point to consider.

Ethics

Ethics Committee Approval: Our study is based on a web research therefore ethical approval did not obtained.

Informed Consent: This study does not include any patient, for this reason there was no need to obtain an informed consent form.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.G., Ç.B., Concept: S.B., G.A., Design: V.H., S.B., Data Collection or Processing: T.G., Ç.B., Analysis or Interpretation: S.B., G.A., Literature Search: V.H., S.B., Writing: T.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Deal SB, Alseidi AA. Concerns of Quality and Safety in Public Domain Surgical Education Videos: An Assessment of the Critical View of Safety in Frequently Used Laparoscopic Cholecystectomy Videos. J Am Coll Surg 2017;225:725-30.
2. Raikos A, Waidyasekara P. How useful is YouTube in learning heart anatomy? Anat Sci Educ 2014;7:12-8.
3. Pitcher GS, Newton DH, Amendola MF. Common Femoral Artery Access on YouTube: What Practices are Being Shown and Who is Delivering the Message? J Surg Educ 2017;74:455-8.
4. Pandey A, Abdullah K, Drazner MH. Impact of Vice President Cheney on public interest in left ventricular assist devices and heart transplantation. Am J Cardiol 2014;113:1529-31.
5. Chen HM, Hu ZK, Zheng XL et al. Effectiveness of YouTube as a Source of Medical Information on Heart Transplantation. Interact J Med Res 2013;2:e28.
6. Agrawal H, Wright OK, Carberry KE, et al. Family perception of unmet support needs following a diagnosis of congenital coronary anomaly in children: Results of a survey. Congenit Heart Dis 2017;12:721-5.
7. Panhuyzen-Goedkoop NM, Wellens HJ, Piek JJ. Early recognition of sudden cardiac arrest in athletes during sports activity. Neth Heart J 2018;26:21-5.
8. Bademci MS, Yazman S, Gunes T, et al. YouTube as a potential source of information on deep venous thrombosis. Phlebology 2017;32:543-7.
9. Gunes T, Serinken M, Alur I, et al. YouTube as a source of information on varicose veins. Phlebology 2016;31:501-5.
10. Azer SA, AlGrain HA, AlKhelaif RA, et al. Evaluation of the educational value of YouTube videos about physical examination of the cardiovascular and respiratory systems. J Med Internet Res 2013;15:e241.
11. Desai T, Shariff A, Dhingra V, et al. Is content really king? An objective analysis of the public's response to medical videos on YouTube. PLoS One 2013;8:e82469.
12. Chen YY, Chen L, Huang TS, et al. Significant social events and increasing use of life-sustaining treatment: trend analysis using extracorporeal membrane oxygenation as an example. BMC Med Ethics 2014;15:21.
13. Hazzam J, Lahrech A. Health Care Professionals' Social Media Behavior and the Underlying Factors of Social Media Adoption and Use: Quantitative Study. J Med Internet Res 2018;20:e12035.
14. Madathil KC, Rivera-Rodriguez AJ, Greenstein JS, Gramopadhye AK, et al. Healthcare information on YouTube: A systematic review. Health Informatics J 2015;21:173-94.
15. Godwin HT, Khan M, Yellowlees P. The Educational Potential of YouTube. Acad Psychiatry 2017;41:823-7.
16. Zimmermann M, Jucks R. Investigating the Role of Communication for Information Seekers' Trust-Related Evaluations of Health Videos on the Web: Content Analysis, Survey Data, and Experiment. Interact J Med Res 2018;7:e10282.
17. Hucíková A, Babic A. Medical Informatics Idle YouTube Potential. Stud Health Technol Inform 2017;238:132-5.

EJCM 2019;7(1):36-38

DOI: 10.32596/ejcm.galenos.2018.00011

Create a Syndrome When Treating a Disease: Acquired Lutembacher Syndrome

Çağlar Kaya, Muhammet Gürdoğan, Servet Altay

Trakya University Faculty of Medicine, Department of Cardiology, Edirne, Turkey

Abstract

Combination of atrial septal defect (ASD) and mitral stenosis (MD) is defined as Lutembacher syndrome (LS). MD is mostly acquired (rheumatic heart disease), as congenital MD is very rare. The percutaneous interventions for MD have become widespread. The ASD may become either congenital or iatrogenic. The coexistence of spontaneous or iatrogenic ASD and acquired MD is known as acquired LS. Here, we report a case of acquired LS.

Keywords: Atrial septal defect, congenital hearth disease, Lutembacher syndrome

Introduction

Congenital atrial septal defect (ASD) and rheumatic mitral stenosis (MD) was first reported in a female patient by Lutembacher in 1916[1]. Lutembacher syndrome (LS) occurs as a rare combination of congenital secundum ASD and an acquired MD[2]. Hemodynamic effects of these two diseases are very interesting. ASD decreases left atrial pressure and mitral valve gradient while MD increases the left to right pass due to ASD. The wide range of ASD plays a role in the relief of symptoms related to MD. The widespread percutaneous interventions have increased this rare combination. We present a 48-year-old woman with a previous percutaneous mitral balloon valvuloplasty (PMBV) history.

Case Report

A 48-year-old female patient was referred to our cardiology clinic with dyspnoea and quick fatigue. Patient history showed PMBV for rheumatic MS in 2014 and hypertension. At the first evaluation, her blood pressure was 110/65 mmHg, and his heart rate was 98 bpm, respectively.

Address for Correspondence: Çağlar Kaya, Trakya University Faculty of Medicine, Department of Cardiology, Edirne, Turkey
Phone: +90 555 604 06 04 **e-mail:** caglarkaya2626@gmail.com **ORCID ID:** orcid.org/0000-0002-2968-5352
Received: 10.05.2018 **Accepted:** 11.06.2018

Cite this article as: Kaya Ç, Gürdoğan M, Altay S. Create a Syndrome When Treating a Disease: Acquired Lutembacher Syndrome. EJCM 2019;7(1):36-38.
DOI: 10.32596/ejcm.galenos.2018.05011

Physical examination revealed a systolic murmur of 3/6° in the mesocardiac area and a diastolic murmur of 3/6° in the apical area. Twelve-lead-electrocardiography showed atrial fibrillation. Transthoracic echocardiography found that the left ventricular ejection fraction was preserved, and revealed calcified and thickened mitral valve, mild mitral regurgitation, moderate tricuspid regurgitation with a pulmonary systolic pressure of 40 mmHg and suspicious view at interatrial septum. Mitral valve area was 1.2 cm^2 according to the pressure half-time method. To minimize the risk of miscalculations due to decreased left atrial pressure we also calculated as 1.3 cm^2 with the planimetry method. The mean diastolic transvalvular mitral valve gradient was 7 mmHg. There was no information about ASD in previous echocardiography reports. Transesophageal echocardiography (TEE) was performed to the patient because of the suspicious view at interatrial septum. TEE revealed rheumatic mitral valve and moderate MD (Figure 1). A small ASD was observed in the 2D TEE and contrast echocardiography (Figures 2 and 3). ASD defect measured 6 mm. Having a history of PMBV no information about ASD in previous report and this new evidence was diagnosed with acquired LS. This is thought to have arisen iatrogenically due to PMBV in 2014 and/or spontaneously due to extreme tension of the left atrium. We took the patient to medical treatment and intensive follow-up.

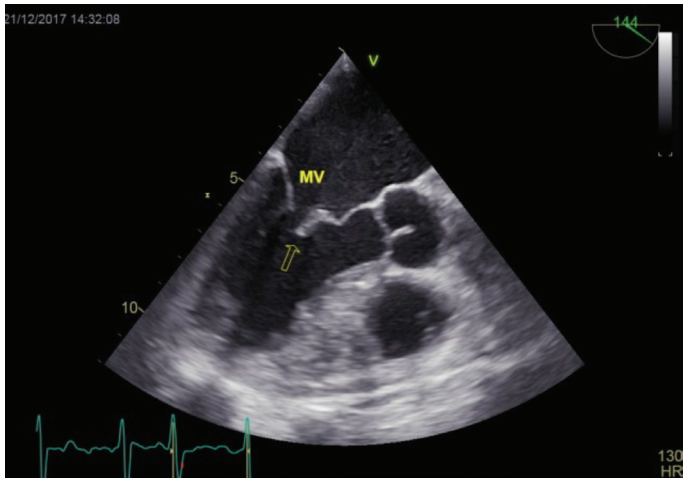


Figure 1. Rheumatic mitral valve and moderate mitral stenosis (transesophageal echocardiography)

Written informed consent was obtained from the patient.

Discussion

LS can be defined as the combination of ASD and MS. Since both ASD and MS are frequently found in women, LS also occurs more commonly among women[3]. Hemodynamic associations between ASD and MS are clinically challenging. As in LS, one can change the clinical and hemodynamic effects of the other. His is due to ASD diameter, severity of MD and right ventricular function. The coexistence of MS and ASD has a distinct course as compared with isolated MS. The existence of ASD in an

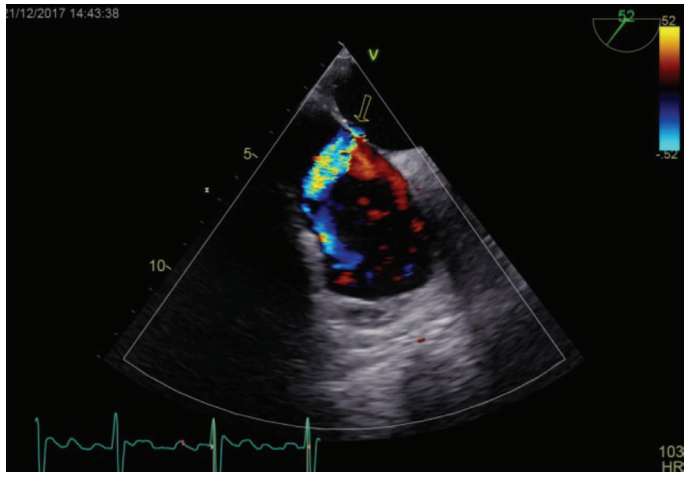


Figure 2. A small atrial septal defect with color imaging (transesophageal echocardiography)

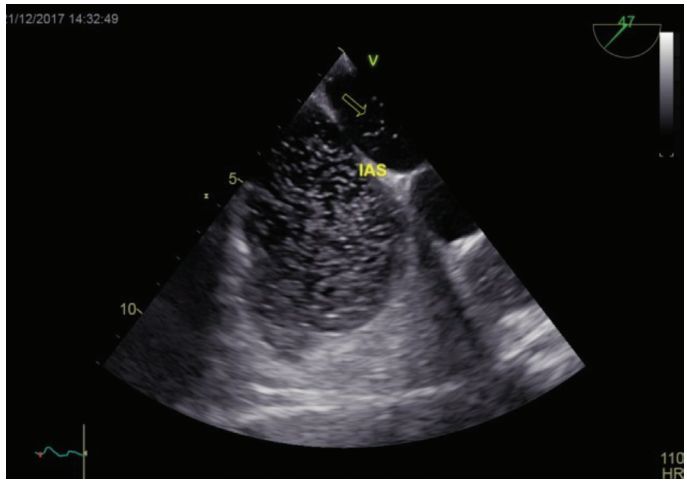


Figure 3. A small atrial septal defect with contrast echocardiography (transesophageal echocardiography)

MS patient, can mimic the symptoms and auscultatory findings of the disease. Increased left-atrial pressure due to MS, increases the left-to-atrial shunt, causing early right-heart failure and pulmonary hypertension. The spread of percutaneous interventions for MD and the occurrence of iatrogenic disorders associated with these interventions led to different definitions for the disease. This condition, "acquired LS", may result from two different scenarios. In the first scenario, in isolated MS patients, an "iatrogenic ASD" may occur due to PMBV, which is performed through atrial septal puncture by the transseptal approach[4]. The second scenario for "acquired LS" is spontaneous secundum type ASD development due to progressive left-atrial enlargement and pressure over load in the presence of severe MS[4]. If LS is diagnosed early, it is a good prognosis. Patients hospitalized for right-sided heart failure and pulmonary hypertension give excellent results in survival following mitral valve replacement and ASD closure. The object of this case is to remind the clinical variations of this rare syndrome, to better understand the echocardiographic findings and to keep this diagnosis in mind when evaluating patients.

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ç.K., Concept: Ç.K., S.A., Design: Ç.K., M.G., Data Collection or Processing: Ç.K., S.A., M.G., Analysis or Interpretation: Ç.K., S.A., M.G., Literature Search: Ç.K., S.A., M.G., Writing: Ç.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Perloff JK. A Trial Septal Defect in the Clinical Recognition of Congenital Heart Disease. 4th ed. Philadelphia: WB Saunders; 1994. p.233-99.
2. Nagamani AC, Nagesh CM. Lutembacher Syndrome. Chapter 64.In: Vijayalakshmi IB, Syamasundar Rao P, Chugh R. editors. A Comprehensive Approach to Congenital Heart Diseases. 1st ed. India: Jaypee Brothers Medical Publishers; 2013. p. 908-16.
3. Perloff JK. The Clinical Recognition of Congenital Heart Disease. 4th ed. Philadelphia: WB Saunders; 1994. p.323-8.
4. Ananthasubramaniam K, Iyer G, Karthikeyan V. Giant left atrium secondary to tight mitral stenosis leading to acquired Lutembacher syndrome: a case report with emphasis on role of echocardiography in assessment of Lutembacher syndrome. J Am Soc Echocardiogr. 2001;14:1033-5.

E Journal of Cardiovascular Medicine
Case Report
39
EJCM 2019;7(1):39-42
DOI: 10.32596/ejcm.galenos.2019.00008

Accessory Mitral Valve Misdiagnosed as Hypertrophic Obstructive Cardiomyopathy

Dilay Karabulut[1], Nihan Turhan Çağlar[1], İsmail Bıyık[2], Hülya Cebe[1], Hande Türeli[1], Faruk Aktürk[1]

[1]İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Cardiology, İstanbul, Turkey
[2]Uşak University Faculty of Medicine Training and Research Hospital, Department of Cardiology, Uşak, Turkey

Abstract

Accessory mitral valve tissue (AMVT) is a rare congenital cardiac malformation. It is recognized as a differential diagnosis of left ventricular outflow tract obstruction. Herein, we report a case of AMVT, which was misdiagnosed as hypertrophic obstructive cardiomyopathy.

Keywords: Hypertrophic obstructive cardiomyopathy, accessory mitral valve tissue, cardiomyopathy

Introduction

Accessory mitral valve tissue (AMVT) is an uncommon congenital cardiac malformation, and it is frequently diagnosed during the first decade of life, but rarely detected in adulthood[(1)]. This disease is commonly associated with other congenital cardiac anomalies such as ventricular septal defects, patent ductus arteriosus and transposition of the great arteries[(1)]. AMVT may be detected as an incidental finding or, in some cases, may cause left ventricular outflow tract (LVOT) obstruction. Patients with AMVT and significant LVOT obstruction usually present in the early days or years of life with a heart murmur and symptoms of LVOT obstruction such as exercise intolerance, chest pain on exertion, syncope and/or heart failure[(2,3)]. Symptoms usually manifest when the mean gradient across the LVOT is more than 50 mmHg[(3-5)]. Herein, we report a case of a 47 year old man with AMVT, which was misdiagnosed as hypertrophic obstructive cardiomyopathy (HOCM).

Address for Correspondence: İsmail Bıyık, Uşak University Faculty of Medicine Training and Research Hospital, Department of Cardiology, Uşak, Turkey
Phone: +90 542 417 32 09 **e-mail:** ismailbiyikmd@yahoo.com **ORCID ID:** orcid.org/0000-0003-2869-5759
Received: 29.04.2018 **Accepted:** 02.03.2019

Cite this article as: Karabulut D, Turhan Çağlar N, Bıyık İ, Cebe H, Türeli H, Aktürk F. Accessory Mitral Valve Misdiagnosed as Hypertrophic Obstructive Cardiomyopathy. EJCM 2019;7(1):39-42.
DOI: 10.32596/ejcm.galenos.2019.00008

Case Report

A 47-year-old male patient was referred to our echocardiography laboratory for the evaluation of hypertrophic obstructive cardiomyopathy. He had well-controlled hypertension. Physical examination revealed a faint, grade 2/6, mid-systolic murmur best heard at the left sternal border and not radiating to the neck. The 1st and 2nd heart sounds were normal, and 3rd or 4th heart sound, gallops or rub was not detected. Electrocardiogram was normal. Transthoracic echocardiography (TTE) revealed normal sized cardiac chambers and mild left ventricular hypertrophy. Interventricular septum thickness was 13 mm, posterior wall thickness 12 mm. Systolic anterior motion (SAM) of mitral valve leaflet was not detected on M mode echocardiography. The mean pressure gradient across the LVOT was 30 mmHg and peak pressure gradient was 50 mmHg. The maximum velocity between the aorta and the left ventricle was detected as 3.4 m/sec, which suggested moderate LVOT obstruction. The left ventricular ejection fraction was 65%. Apical four chamber view revealed a small structure attached to the anterior mitral valve leaflet. Transesophageal echocardiography (TEE) revealed a mobile, hyper-echogenic, membrane like structure moving towards LVOT during systole (Figure 1). The structure was attached to the ventricular side of the anterior mitral valve leaflet as a chordae tendineae like structure, which was meeting the description of an AMVT (Figure 1). This structure was probably misdiagnosed as SAM in previous echocardiographic assessments. Three dimensional transesophageal echocardiographic examination (TEE) clearly demonstrated AMVT (Figure 2). Two dimensional color flow Doppler TEE showed trace turbulence in the systolic flow, starting immediately proximal to the lesion (Figure 3). No other congenital heart anomaly was present. The patient has now been following up with medical treatment and has no symptoms.

Informed consent form was obtained from the patient.

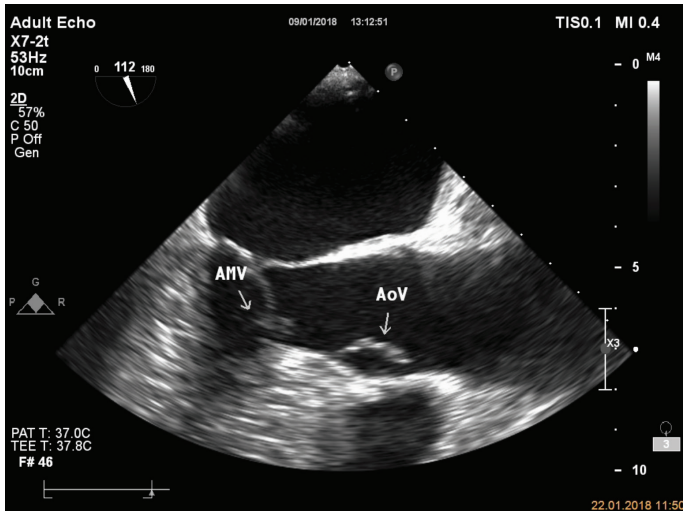


Figure 1. Accessory mitral valve tissue attached to the ventricular side of the anterior mitral valve leaflet

Discussion

AMVT is an uncommon anomaly in adults and may be associated with other congenital intracardiac and

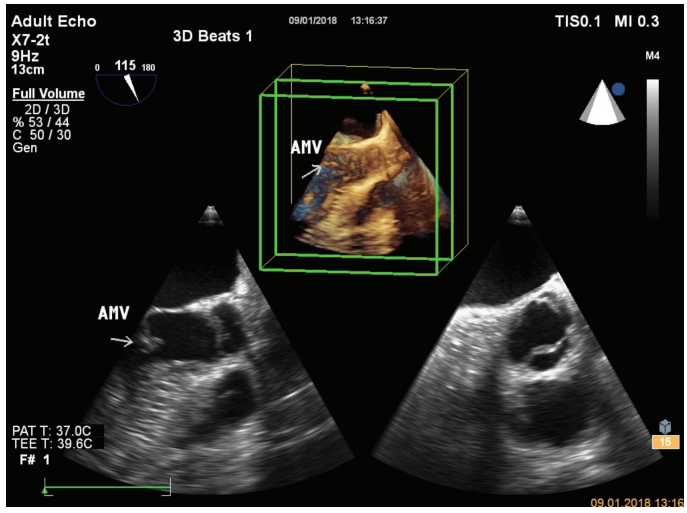


Figure 2. Three dimensional transesophageal echocardiographic image of accessory mitral valve tissue

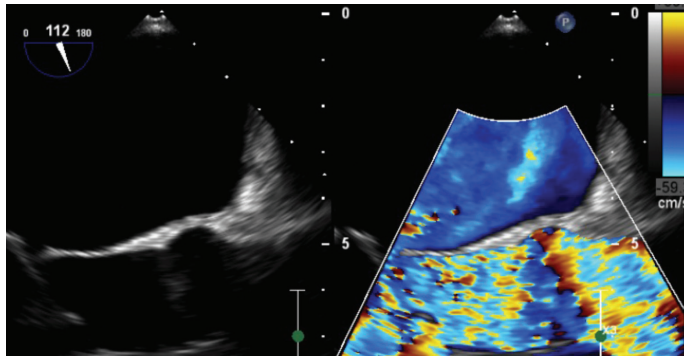


Figure 3. Trace turbulence in systolic flow starting immediately proximal to the lesion

vascular malformations such as atrial septal defects, atrial septal aneurysms, coronary artery anomalies, persistent left superior vena cava, coarctation of aorta, bicuspid aortic valve, cleft mitral valve and/or dextrocardia[1-6]. The estimated incidence of AMVT in adults is about 1: 26.000 echocardiograms[7]. It is more frequently identified in men, this entity has a male to female ratio of 1.75[1]. The embryologic mechanism of AMVT formation is not clear and may be related to abnormal or incomplete separation of the mitral valve from the endocardial cushions[6,8].

AMVT may affect one or both atrioventricular valves simultaneously but the mitral valve is more often involved[8]. Published data show a high prevalence of the mobile type of AMVT, which projects itself into the LVOT, in most cases originating from the anterior mitral valve leaflet, with a higher incidence of parachute like or balloon like structures[6,8,9]. Morphologically, AMVT may be classified as type 1 (fixed) or type 2 (mobile)[6]. Type 1 presents in two forms: 1A (nodular) and 1B (membranous), and type 2 is divided into two subtypes: 2A (pedunculated) and 2B (leaflet like)[6]. The latter corresponds to 46% of cases and may be further subdivided into leaflets with rudimentary chordae and chordae with well-developed tissue[6]. According to this classification, our case meets type 2B. Patients with AMVT may be asymptomatic, and it may be an incidental finding during routine echocardiography. However, the patients may usually become symptomatic when the mean gradient across the LVOT reaches 50 mmHg[7,9,10]. Both TTE and TEE may help in making the diagnosis, and reveal possible associated lesions and complications. Both 3D TTE and 3D TEE enable more definite anatomic characterization, and allow visualization of the accessory tissue attachment to the interventricular septum or the myocardium, which can help in its classification[6,11,12]. 3D TEE provides en face visualization of the mitral valve leaflets from both left ventricular and left atrial aspects.

Regarding to the treatment of this anomaly, cardiac surgery is indicated only in patients with significant LVOT gradients and those undergoing correction of other congenital cardiac defects[10,13]. In our case, because of the presence of left ventricular hypertrophy and LVOT gradient, the patient may have been misdiagnosed as HOCM and AMVT may have incorrectly been assessed as SAM. However, AMVT may be seen together with genetically confirmed hypertrophic cardiomyopathy[9]. Both transthoracic and transesophageal echocardiography and, more recently, 3D echocardiography, play a fundamental role in the diagnosis, management, and follow-up of patients with this anomaly,

Because it is a rarely seen congenital cardiac malformation, AMVT should be kept in mind in the differential diagnosis of SAM in hypertrophic cardiomyopathy with LVOT obstruction.

Ethics

Informed Consent: Informed consent form was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.K., N.T., Concept: N.T., Design: İ.B., Data Collection or Processing: H.C., H.T., Analysis or Interpretation: F.A., Literature Search: D.K., Writing: D.K., N.T., İ.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Yuan SM, Shinfeld A, Mishaly D, Haizler R, Ghosh P, Raanani E. Accessory mitral valve tissue: a case report and an updated review of literature. J Card Surg 2008;23:769-72.
2. Prifti E, Frati G, Bonacchi M, Vanini V, Chauvaud S. Accessory mitral valve tissue causing left ventricular outflow tract obstruction: case reports and literature review. J Heart Valve Dis. 2001;10:774-8.
3. Prifti E, Bonacchi M, Bartolozzi F, Frati G, Leacche M, Vanini V. Postoperative outcome in patients with accessory mitral valve tissue. Med Sci Monit 2003;9:RA126-33.

4. Ascuitto RJ, Ross-Ascuitto NT, Kopf GS, Kleinman CS, Talner NS. Accessory mitral valve tissue causing left ventricular outflow obstruction (two-dimensional echocardiographic diagnosis and surgical approach). Ann Thorac Surg 1986;42:581-4.

5. Popescu BA, Ghiorghiu I, Apetrei E, Ginghina C. Subaortic stenosis produced by an accessory mitral valve: the role of echocardiography. Echocardiography 2005;22:39-41.

6. Manganaro R, Zito C, Khandheria BK, Cusmà-Piccione M, et al. Accessory mitral valve tissue: an updated review of the literature. Eur Heart J Cardiovasc Imaging 2014;15:489-97.

7. Rovner A, Thanigaraj S, Perez JE. Accessory mitral valve in an adult population: the role of echocardiography in diagnosis and management. J Am Soc Echocardiogr 2005;18:494-8.

8. Yoshimura N, Yamaguchi M, Oshima Y, et al. Clinical and pathological features of accessory valve tissue. Ann Thorac Surg 2000;69:1205-8.

9. Musumeci B, Spirito P, Parodi MI, Assenza GE, Autore C. Congenital accessory mitral valve tissue anomaly in a patient with genetically confirmed hypertrophic cardiomyopathy. J Am Soc Echocardiogr 2011;24:592.e5-6

10. Panduranga P, Eapen T, Al-Maskari S, Al-Farqani A. Accessory mitral valve tissue causing severe left ventricular outflow tract obstruction in a post-Senning patient with transposition of the great arteries. Heart Int 2011;6:e6.

11. Mizuno A, Koike Y, Niwa K. Four-dimensional visualization of accessory mitral valve tissue and cleft mitral valve movement. Echocardiography 2013;30:E114-5.

12. Kim MS, Klein AJ, Groves BM, Quaife RA, Salcedo EE. Left ventricular outflow tract obstruction in the presence of asymmetric septal hypertrophy and accessory mitral valve tissue treated with alcohol septal ablation. Eur J Echocardiogr 2008;9:720-4

13. D'Aloia A, Vizzardi E, Chiari E, et al. Dynamic mild subaortic left ventricular obstruction caused by an accessory mitral valve attached to the anterior mitral valve in a young pregnant woman. Eur J Echocardiogr 2008;9:160-1.

E Journal of Cardiovascular Medicine
Case Report
43
EJCM 2019;7(1):43-46
DOI: 10.32596/ejcm.galenos.2019.00032

A Huge Aneurysm of the Ascending Aorta in a Young Male with Marfan Syndrome: "Giant Aorta-Great Heart"

Ersin Çağrı Şimşek[1], Ezgi Özyol Us[1], Mine Tavlı[2], Öner Özdoğan[1]

[1]University of Health Sciences, İzmir Tepecik Training and Research Hospital, Clinic of Cardiology, İzmir, Turkey
[2]University of Health Sciences, İzmir Tepecik Training and Research Hospital, Clinic of Cardiovascular Surgery, İzmir, Turkey

Abstract

Marfan syndrome, described in the 19th century, is a connective tissue disease inherited as an autosomal dominant, owing to mutations in the *FBN1* gene encoding fibrillin-1. Marfan syndrome involves the cardiovascular, ocular, and skeletal systems. Although Marfan syndrome is inherited as an autosomal dominant with high penetrance, about 30% of cases are due to sporadic mutation. A 34-year-old man with no prior medical history presented with worsening exercise dyspnea. On physical examination, he was tall stature, he had myopia, pectus deformity, pes planus, the wrist and thumb signs. His cardiac examination revealed a grade 3/6 early diastolic murmur over the aortic area. Transthoracic echocardiography revealed a severely dilated left ventricle (left ventricular end diastolic diameter and volume; 9.0 cm, 520 mL respectively), a giant ascending aorta measuring 11.0 cm and reduced systolic function (left ventricular ejection fraction 50%). A computed tomography angiography imaging which was ordered to exclude aortic dissection and assess the extent of aortic dilation showed an aortic diameter of 11.6x11 cm at the widest point without any dissection flap. The patient was diagnosed as having Marfan syndrome according to the Ghent criteria and underwent Benthall procedure. In the literature, huge aneurysm of the ascending aorta without dissection is extremely rare, and the current case with a giant aneurysm of approximately 12 cm has been treated uneventfully. In conclusion, such huge aortic aneurysms could be asymptomatic and silent for many years until severe aortic regurgitation and aortic dissection occurs.

Keywords: Ascending aorta, giant aneurysm, aortic dilatation, Marfan syndrome, genetics

Address for Correspondence: Ersin Çağrı Şimşek, University of Health Sciences, İzmir Tepecik Training and Research Hospital, Clinic of Cardiology, İzmir, Turkey
Phone: +90 232 469 69 69-3666 **e-mail:** ercagsim@hotmail.com **ORCID ID:** orcid.org/0000-0001-6084-0982
Received: 30.05.2018 **Accepted:** 02.03.2019

Cite this article as: Şimşek EÇ, Özyol Us E, Tavlı M, Özdoğan Ö. A Huge Aneurysm of the Ascending Aorta in a Young Male with Marfan Syndrome: "Giant Aorta-Great Heart". EJCM 2019;7(1):43-46.
DOI: 10.32596/ejcm.galenos.2019.00032

Introduction

Marfan syndrome (MFS), described in the 19th century, is a connective tissue disease inherited as an autosomal dominant, owing to mutations in the *FBN1* gene encoding fibrillin 1[1]. MFS involves the cardiovascular, ocular, and skeletal systems; therefore, it is characterized by those three clinical criteria; thoracic aortic aneurysm and/or dissection, ectopia lentis, and systemic features (with score ≥7)[2].

In this report, we described a new diagnosed MFS case which has an overly dilated heart owing to severe aortic insufficiency with huge aortic aneurysm

Case Report

A 34-year-old man with no prior medical history presented with worsening exercise dyspnea and marked limitation in activity due to symptoms for the previous three weeks. Among his family members, nobody had an aortic disease and connective tissue disease. A month prior to the admission he was easily climbing up the fifth floor. On physical examination, he was 184 cm tall, weighed 79 kg, and he had myopia, pectus deformity, pes planus, and elongated limbs (arm span 194 cm). Another finding of the physical examination was wrist sign (thumb and fifth digit overlap when around the wrist) (Figure 1). His cardiac examination revealed a grade 3/6 early diastolic murmur over the aortic area. Chest X-ray showed mild cardiomegaly and mediastinal enlargement (Figure 2). The patient underwent an echocardiogram that showed a quite dilated left ventricle, severe aortic valve insufficiency, and over-dilated aortic root involving the ascending aorta. Transthoracic echocardiography revealed a severely dilated left ventricle (left ventricular end-diastolic dimension: 9.0 cm, left ventricular end-diastolic volume: 520 mL), a giant ascending aorta measuring 11.0 cm and reduced systolic function (left ventricular ejection fraction: 50%) (Figure 3). A cardiovascular computed

Figure 1. Skeletal characteristics of the patient: A) pectus deformity, B) striae atrophicae in axillary region, C) pes planus, D) the wrist sign, E) the wrist sign and arachnodactyly, F) the thumb sign

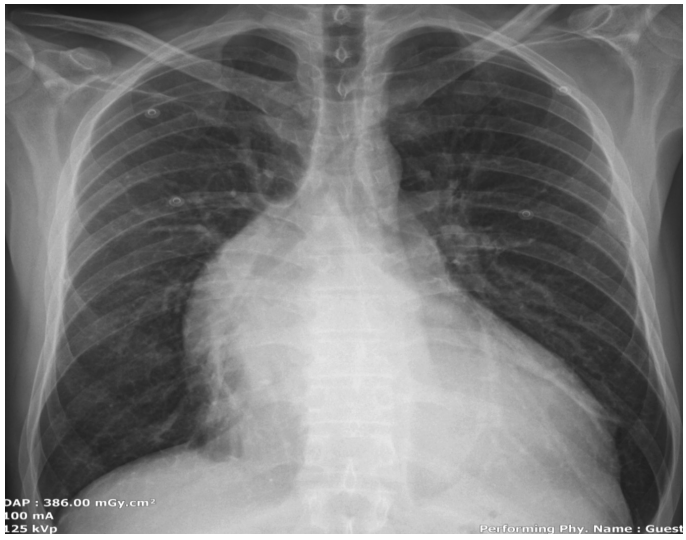


Figure 2. Chest X-ray showing cardiomegaly and mediastinal enlargement in right paracardiac area

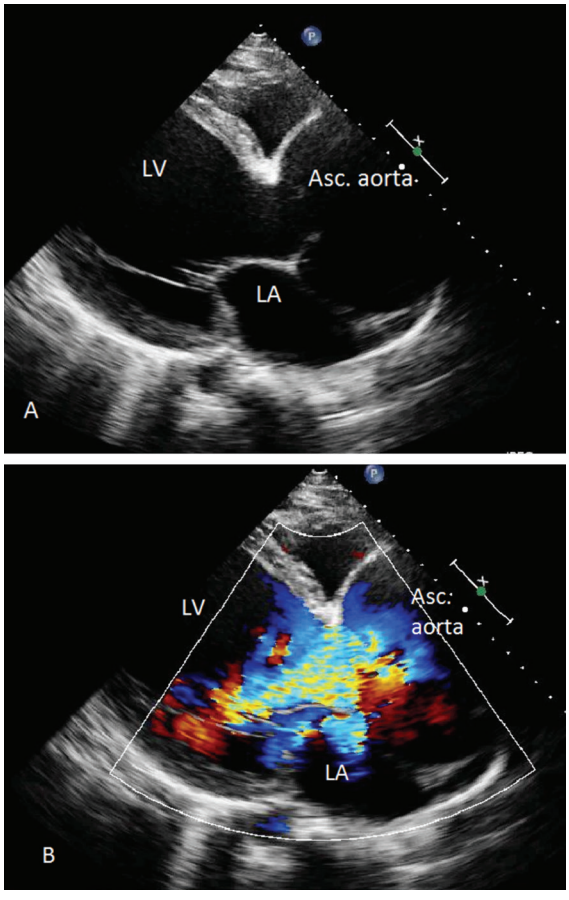


Figure 3. Transthoracic echocardiography parasternal long axis view shows, A) dilated left ventricle and ascending aortic aneurysm and, B) severe aortic regurgitation
Asc.: Ascendan, LA: Left atrium, LV: Left ventricle

tomography angiography (CTA) imaging study was ordered to exclude aortic dissection and assess the extent of aortic root dilation. A CTA showed an aortic diameter of 11x11.6 cm at the widest point without any dissection flap (Figures 4 and 5). Written informed consent was obtained from the patient who underwent elective surgery.

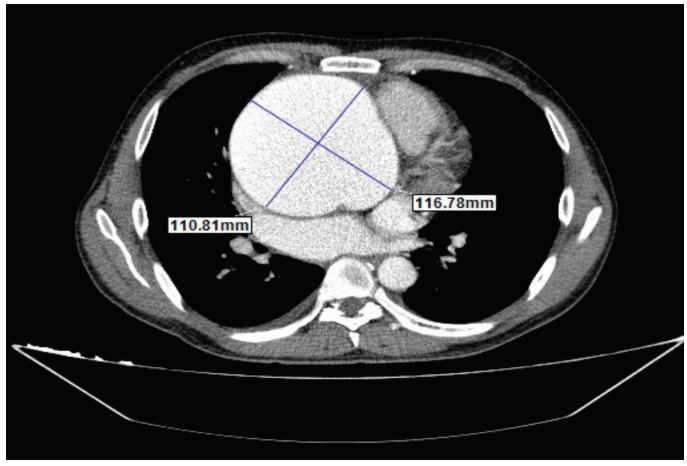


Figure 4. Computed tomography aortogram showing the dimension of ascending aorta about 110x116 mm

Figure 5. Computed tomography aortogram with 3D reconstruction showing fusiform dilatation involving sino-tubular junction, ascending aorta, proximal aortic arch

The patient was diagnosed as having MFS according to the Ghent criteria and underwent Benthall procedure which involves replacement of the aortic root with a mechanical valved conduit. Following the postoperative course, he was discharged uneventfully with warfarin, metoprolol, and ramipril on the seventh day.

Discussion

Although MFS is inherited as an autosomal dominant with high penetrance, about 30% of cases are due to sporadic mutations[3]. The prevalence of MFS was reported ranging between 1/5.000-1/10.000. Cardiovascular manifestations include thoracic aortic aneurysm/dissection, aortic regurgitation from the aortic root impairment, and the mitral insufficiency with mitral valve prolapses. Although aortic dilatation is progressive throughout life, losartan and beta-blockers reduce the rate of dilatation, aortic dissection, and heart failure[4]. The incidence of ascending aortic aneurysms, defined as giant aneurysms greater than 10 cm in diameter, is increasing in MFS. Guidelines recommended aortic imaging of first-degree relatives in patients with familial aortic aneurysms. The current European Society of Cardiology guidelines recommended prophylactic surgery in patients with MFS, who have a maximal aortic diameter ≥50 mm. The factors that would lead to surgical repair at ≥45 mm include a family history of dissection, size increase 3 mm/year, severe aortic regurgitation, or desire for pregnancy[5].

In the case reported, the reason that the patient became symptomatic is the presence of severe aortic valve regurgitation due to aortic root dilatation. Although the patient admitted the hospital before dissecting the aorta which is the most feared complication of MFS, the systolic function of heart was reduced and left ventricular diameters were greatly enlarged owing to severe aortic regurgitation. Despite a negative family history, the current-reported-case was sporadic. In suspicious cases, even if there is negative family history, genetic test and systemic features of MFS should be examined well and the criteria of MFS should be kept in mind. In the literature, huge aneurysm of the ascending aorta without dissection is extremely rare, and the current case with a giant aneurysm of approximately 12 cm has been treated uneventfully.

In conclusion, such huge aortic aneurysms could be asymptomatic and silent for many years until severe aortic regurgitation and aortic dissection occurs.

Ethics

Informed Consent: Written informed consent was obtained from the patient who underwent elective surgery.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.T., Concept: E.Ç.Ş., Ö.Ö., Design: E.Ç.Ş., Ö.Ö., Data Collection or Processing: E.Ç.Ş., E.Ö.U., M.T., Analysis or Interpretation: E.Ç.Ş., Ö.Ö., Literature Search: E.Ç.Ş., E.Ö.U., Writing: E.Ç.Ş., E.Ö.U.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Ramirez F, Dietz HC. Marfan syndrome: from molecular pathogenesis to clinical treatment. Curr Opin Genet Dev. 2007;17:252-8.
2. Loeys BL, Dietz HC, Braverman AC, et al.The revised Ghent nosology for the Marfan syndrome. J Med Genet. 2010;47:476-85.
3. Toudjarska I, Kilpatrick MW, Lembessis P, et al. Novel approach to the molecular diagnosis of Marfan syndrome: application to sporadic cases and in prenatal diagnosis. Am J Med Genet. 2001;99:294-302.
4. Stuart AG, Williams A. Marfan's syndrome and the heart. Arch Dis Child. 2007;92:351-6.
5. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2014;35:2873-926.

E Journal of Cardiovascular Medicine

Letter to the Editor

47

EJCM 2019;7(1):47-48

DOI: 10.32596/ejcm.galenos.2018.00051

Abdominal Aorta Hypoplasia: A Rare Aortic Anomaly

Tülay Demircan[1], Onur Işık[2], Barış Güven[1], Muhammet Akyüz[2]

[1]University of Health Sciences, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Cardiology, İzmir, Turkey
[2]University of Health Sciences, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Cardiovasculary Surgery, İzmir, Turkey

Dear Editor,

Abdominal aortic hypoplasia is very rare anomaly seen in the literature[1,2]. There are only few case presentations for this diagnosis. Etiological reasons are less known. But these include developmental defects, infectious, inflammatory causes and genetic syndromes such as neurofibromatosis, Williams Bauren syndrome and hypomelanosis Ito[3,4]. In this article we present rare cases images of abdominal aortic hypoplasia. A 3-year-old girl was referred to our clinic with hypertension. Previous history was insignificant. The patient complained post-prandial pain and extremity pain. On physical examination, body weight and height were 10 kg (<3 percentile), 75 cm (<3 percentile), respectively. There were no skin manifestations or dismorphic signs or mental retardation. Pulse rate was 110/min; blood pressure was measured from the right lower extremity 85/51 mmHg, from the right upper extremity 110/68 mmHg. Her general condition was good. Chest X-ray and electrocardiogram were normal. Blood tests were normal including renal function parametars. These findings make think that the patient might have the aortic coarctation. Echocardiography was assessed as normal. Thoracic computed tomography angiography was revealed doubtful image of stenosis of T12 segment at descending aorta (Figure 1). Catheter angiography was performed. The catheter was inserted into the aorta via the femoral artery and an opaque material injection was performed. All of the segments of the abdominal aorta starting from the mid-thoracic aortic level appeared to be the hypoplastic. A multiple colleteral vessels were observed (Figure 2). A large Riolan arcade was noted. Both iliac arteries were mildly hypoplastic. The procedure was terminated immediately to ensure that the circulation of the nourished region was not impaired. Nevertheless a color change was observed starting from the inguinal till to the umbilical region. About an hour later, the color change was disappeared. All with these findings, the patient was diagnosed with abdominal aortic hypoplasia. Because of asymtomatic nature of diagnosis, the patient scheduled for clinical follow-up and started the antihypertensive medication as nifedipin. However, if renal insuffiency, mesenteric ischemia, medically uncontrolled hypertension, and leg claudication were present, it was

Address for Correspondence: Tülay Demircan, University of Health Sciences, İzmir Tepecik Training and Research Hospital, Clinic of Pediatric Cardiology, İzmir, Turkey
Phone: +90 505 753 87 60 **e-mail:** tulay.sirin@hotmail.com **ORCID ID:** orcid.org/0000-0002-2529-2906
Received: 17.10.2018 **Accepted:** 19.12.2018

Cite this article as: Demircan T, Güven B, Işık O, Akyüz M. Abdominal Aorta Hypoplasia: A Rare Aortic Anomaly. EJCM 2019;7(1):47-48.
DOI: 10.32596/ejcm.galenos.2018.00051

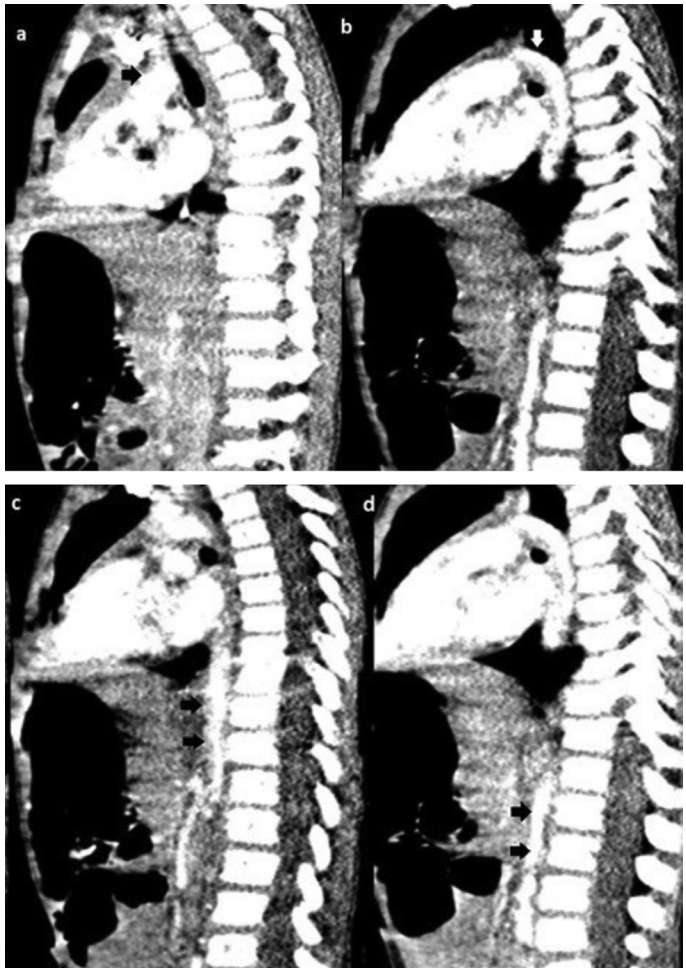


Figure 1. Computed tomography angiography in case showing diffuse narrowing of the descending thoracic and abdominal aorta (arrows)

informed that surgery could be recommended to relieve the patient's symptoms.

Ethics

Peer-review: Externally peer-reviewed.

Figure 2. All segment of the abdominal aorta from the mid-thoracic aortic level appeared to be the hypoplastic. A multiple colleteral vessels were observed

References

1. Coutance G, Labombarda F, Cauderlier E, Richard P, Bonne G, Chapon F. Hypoplasia of the aorta in a patient diagnosed with LMNA gene mutation. Congenit Heart Dis 2013;8:127-9.
2. Grebeldinger SP, Balj SS, Adic O. Severe diffuse hypoplasia of the aorta associated with multiple vascular abnormalities. Vascular 2011;19:170-4.
3. Terramani TT, Salim A, Hood DB, Rowe VL, Weaver FA. Hypoplasia of the descending thoracic and abdominal aorta: a report of two cases and review of the literature. J Vasc Surg 2002;36:844-8.
4. Paşaoglu L, Toprak U, Akdal B, Acar D, Koparal S. Abdominal Aortic Hypoplasia, a Rare Cause of Hypertension. British Journal of Medicine & Medical Research 2015-7:789-94.

DOI: 10.32596/ejcm.galenos.2019.e001

DOI: 10.15511/ejcm.18.00252

Keskin Ö, Sipahi M, Tokgöz VY, Takır S, Fındık Güvendi G. The effect of benfothiamin and vitamın D in ischemia / Reperfusion model of rat skeletal muscle. EJCM 2018;6:68-74. DOI: 10.15511/ejcm.18.00252

These mistakes have made by author inadvertently. The errors correction in the article has been demonstrated in the following list:

Error

Özlem Keskin[1], Mehmet Sipahi[1], Vehbi Yavuz Tokgöz[1], Selçuk Takır[2], Gülname Fındık Güvendi[1]

[1)] Giresun University, Department of Obstetri & Gynecology, Asst. Prof., MD:, Giresun, Turkey.
[2)] Giresun University, Department of Obstetri & Gynecology, Assoc. Prof. MD., Giresun, Turkey.

Correction

Özlem Keskin[1], Mehmet Sipahi[2], Vehbi Yavuz Tokgöz[2], Selçuk Takır[3], Gülname Fındık Güvendi[4]

[1]Giresun University Faculty of Medicine, Department of Cardiovascular Surgery, Giresun, Turkey
[2]Giresun University Faculty of Medicine, Department of Obstetrics and Gynecology, Giresun, Turkey
[3]Giresun University Faculty of Medicine, Department of Pharmacology, Giresun, Turkey
[4]Kafkas University Faculty of Medicine, Department of Pathology, Kars, Turkey