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Surgeries and Cardiovascular System

Highlights

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Comparative Retrospective Study

Central Retinal Artery Occlusion

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VOLUME 23 ISSUE 2 VERSION 1.0

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Surgeries and Cardiovascular System

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Central Retinal Artery Occlusion and its Visual Prognosis in an African Population-Analytical Comparative Retrospective Study

By Francis Kwasi Obeng, Vipan Kumar Vig, Preetam Singh, Rajbir Singh & Baaba Dennis

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Aim: To assess visual prognosis of large series of patients after being diagnosed with CRAO.

Materials and Methods: Records of patients who had been managed for CRAO were reviewed retrospectively for safety, complication, visual outcome and prognosis. Patients' demographic data, indications of treatment and length of follow up were collected and analysed using Chi square and paired t-tests.

Results: A total of 40 eyes of 40 patients (15 females and 25 males) were identified. Mean age at diagnosis was 70.4 +3.5 (range68-75 years) with minimum follow up period of 5 years (range 5 – 8).Visual acuities were poor in all eyes 40 (100%). Ten patients (25%) died from various cardiovascular diseases.

Keywords: *retinal artery occlusion, sudden loss of vision, ocular emergency, eye stroke, artery occlusion, myocardial infarction, cerebrovascular accident, stroke.*

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Francis Kwasi Obeng [α], Vipan Kumar Vig [σ], Preetam Singh [ρ], Rajbir Singh [ω] & Baaba Dennis [¥]

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Conclusion: Visual prognosis of CRAO is generally poor. No treatment can help regain vision in the affected eye. Timely management of systemic underlying disease prevents CRAO in contralateral eye and mortality.

Keywords: retinal artery occlusion, sudden loss of vision, ocular emergency, eye stroke, artery occlusion, myocardial infarction, cerebrovascular accident, stroke.

I. Introduction

Though uncommon with incidence rate of 1 to 2 in 100,000 people globally per year (py) [1], CRAO is an ocular emergency with ability to cause rapid irreversible visual loss and deterioration [2], a manifestation which could be omen for mortality in those affected. In some Asian countries the incidence is 6 in 100,000 people py [3]. In the USA, it is 2 in 100,000 py [4]. The magnitude of the problem has not been well established in Africa due to paucity of research in that field. However, in the study hospital in Ghana it is 2 in 100,000 py.

The most common aetiology as determined by scientific studies is ipsilateral internal carotid artery stenosis [5]. The heart, aortic arch and great vessels may throw emboli to the central retinal artery and cause the disease [6]. Findings from the EAGLE study corroborate the fact that cardiovascular risk factors like obesity, hypertension, tobacco use, hypercholesterolemia and diabetes are the major risk factors associated with the disease [7]. There are three major events capable of leading to CRAO: embolism, in situ thrombosis and vascular spasm with the former being the most common. Emboli may be formed from cholesterol, calcium and platelet-fibrin [8].Other overlooked, yet common embolus forming agents include fat from fracture of long bones, sickled cells, amniotic fluid, metastatic cells from tumours, gestational trophoblastic disease, septic cells from endocarditis, hepatic hydatid cyst, particulate material from intravenous injection, foreign material from catheter insertion, gas from central venous cannulation surgery and chemotherapy [9].

CRAO-associated thrombi may be caused by atherosclerosis, collagen-vascular disease, inflammatory, and/or hypercoagulable states. Diseases like polycythemia vera, sickle cell anemia, multiple myeloma, systemic lupus erythematosus, factor V Leiden, prothrombin III mutation, hyperhomocysteinemia, polyarteritis nodosa, giant cell (temporal) arteritis, antiphospholipid syndrome, activated protein C resistance, Behcet disease, and syphilis are therefore causes of CRAO. Appropriate clinical judgment to differentiate thromboembolic from arteritic processes is crucial as rapid treatment with steroids for vasculitis is associated with improved outcomes in CRAO [8].

Pathophysiologically, occlusion of the central retinal artery results in retinal ischemia, vision loss, and eventual necrosis. Additionally, there is retinal edema with pyknosis of the ganglion cell nuclei. Progression of the ischaemia makes the retina become opacified and yellow-white in appearance. Research has proved that incomplete CRAO, permanent retinal damage occurs in just over 90 minutes [8]. In the clinical setting where occlusion may be partial, the return of vision may be achieved after 8 to 24 hours. Approximately 15% of the general population has significant macular collateral circulation from the cilioretinal artery. Patients with this anatomical variant typically may have less severe presentations and better long-term prognoses [8]. Typically, the clinical features of CRAO include sudden, painless, monocular vision loss that occurs over seconds characterized by relative afferent pupillary

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defect, box-carring, cherry red spot and pale retina (fig 2 and 3).

Once an individual develops CRAO, there is no standard therapeutic intervention which can be used to improve vision in the affected eye [10]. Non-invasive treatments used without success include ocular massage, hyperbaric oxygen (HBOT), carbogen inhalation, intraocular pressure reduction, anticoagulation, sublingual isosorbide dinitrate (SISDN) and systemic steroid. Invasive therapies, some of which made sight in the affected eye worse, include anterior chamber paracentesis [11], laser embolectomy [12], pars plana vitrectomy with direct central retinal artery massage [13] and intraarterial thrombolysis [14].

Many are the theories which have been propounded to emphasise that the retina forms part of central nervous system [15]. Characteristics of blood vessels within the brain and retina are therefore similar. As shown in fig 1, the first branch of internal carotid is ophthalmic whose first branch is central retinal artery. Similarly, other arteries branch off from the internal carotid to supply other parts of the brain. An occlusion of retinal artery may be a strong indication that other vessels could be equally occluded in almost all the vital organs in the body (heart, brain, kidney, liver, lung) to cause ischaemia and possible mortality. In fact, it has been scientifically proved that the same atherosclerotic risk factors for peripheral vascular, cerebrovascular and cardiovascular diseases are present in CRAO and these must be timely and properly assessed to prevent mortality, and morbidity in the better eye [16]. Ischaemic stroke and ischemia in general do not have well established treatment and CRAO is not an exception [17,18,19,20].

One of the branches of ophthalmic artery is the cilioretinal artery (CRA) found in 14 to 26% of the general population [21]. It constitutes extra source of blood supply to the macula. The fortunate patients who have CRA maintain their central vision even when they get CRAO [22]. Their peripheral vision, however, remains seriously and irreversibly impaired [16].

To date a few publications have shown several types of unspecific treatment with unfavourable visual prognosis of affected eye in management of CRAO [10,11,12,13,14]. To the best of our knowledge, this is the first time a study is being published to ascertain visual prognosis of cross section of Africans who had CRAO.

The purpose of the study was to analyse visual prognosis of patients in Sub-Sahara Africa who underwent different types of treatment after being diagnosed with CRAO.

II. Materials and Methods

This is an analytical comparative retrospective study carried out from October 2020 to review medical records of 40 patients (40 eyes) who underwent various types of management from September 2013 to September 2021 after being diagnosed with CRAO (fig 2 and 3) in the study hospital.

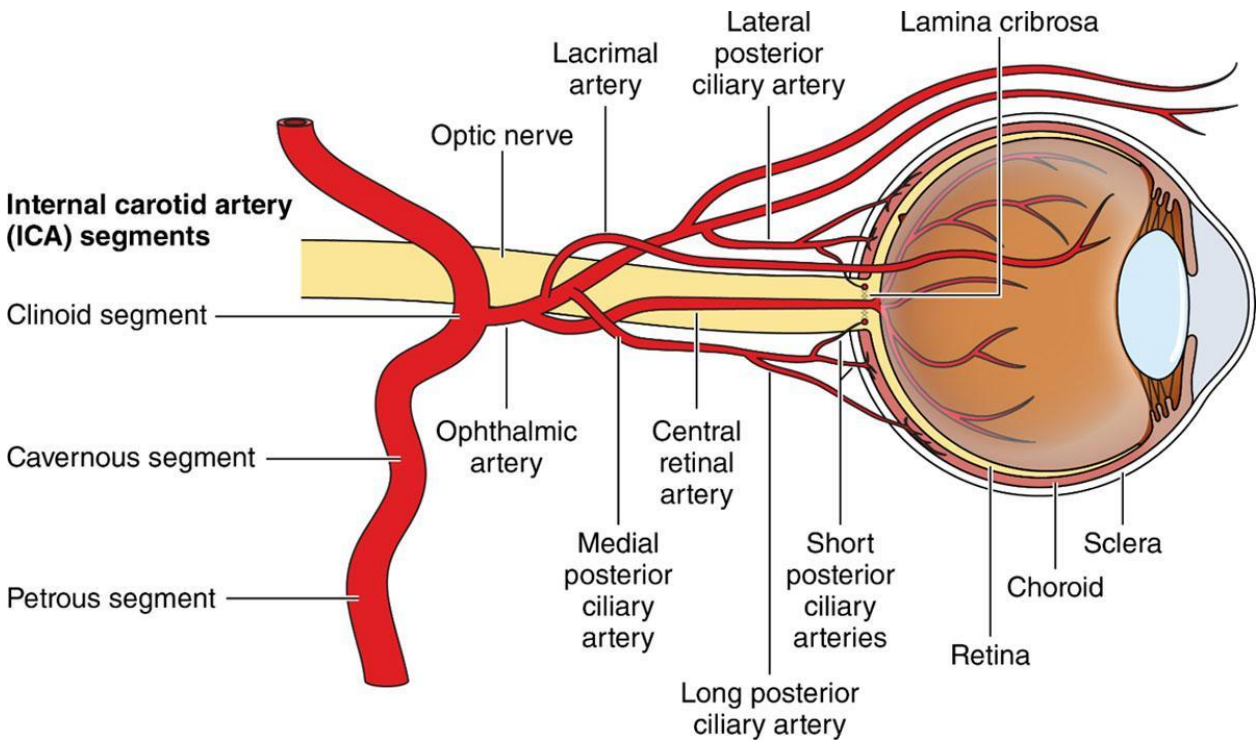

Fig. 1: Origin of central retinal artery from major blood vessel

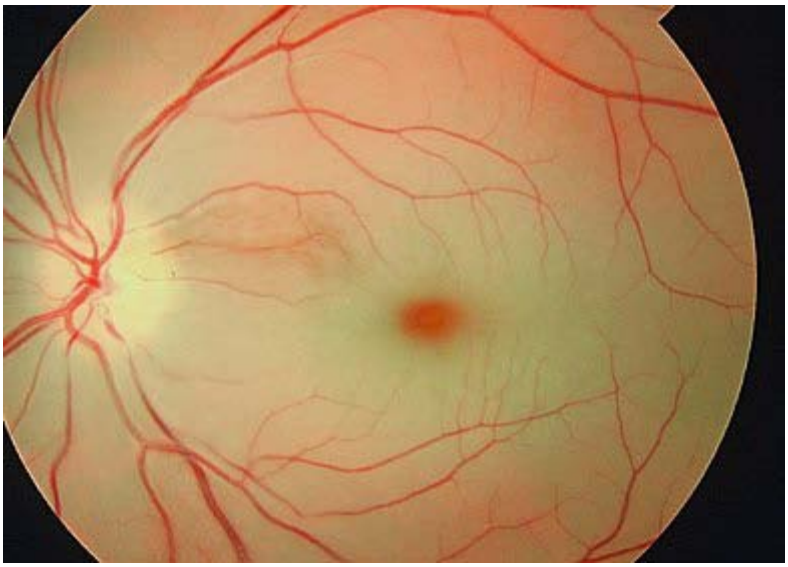

Fig. 2: CRAO with cherry red spot, attenuated blood vessels, pale retina and disc

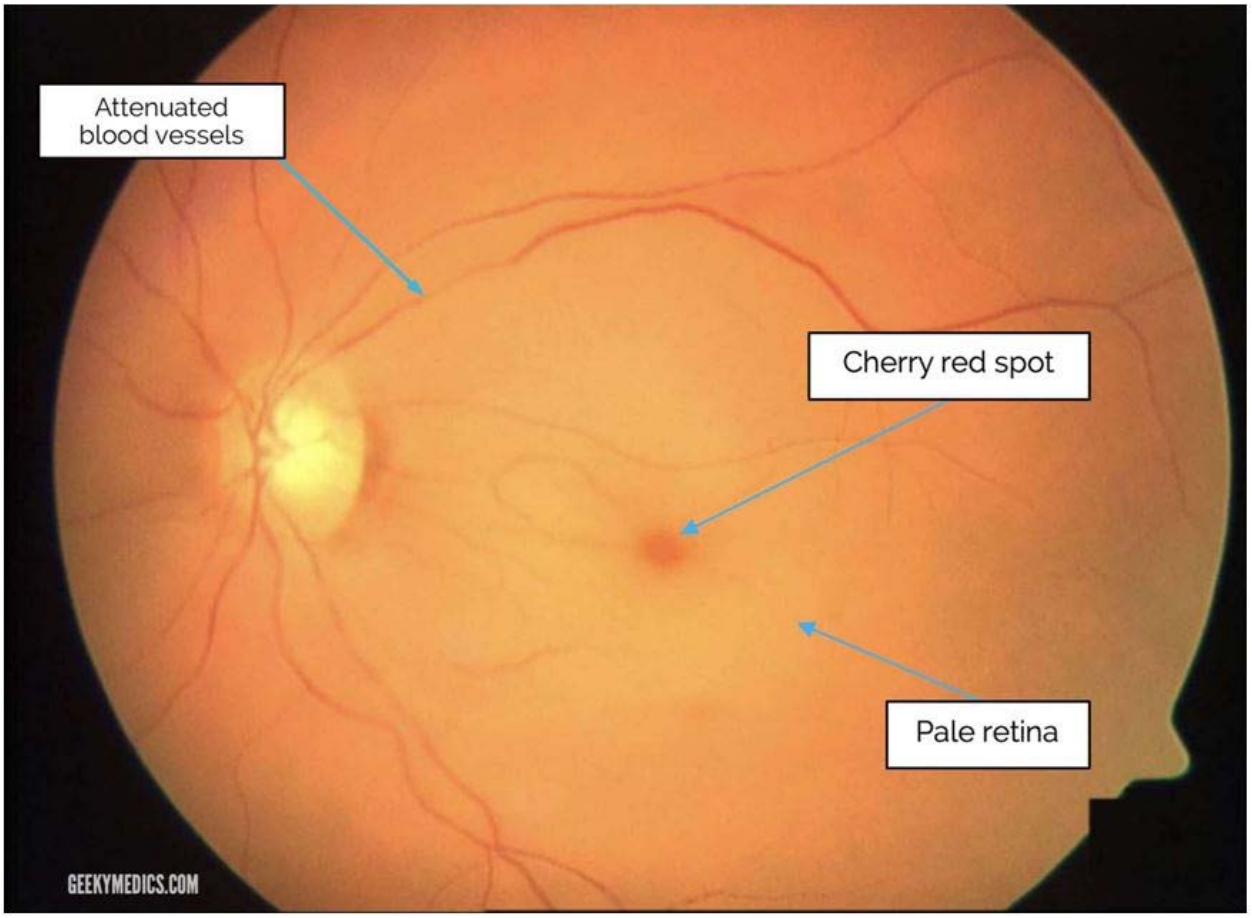

Fig. 3: CRAO

These patients had a minimum follow up of 5 years. One experienced Consultant Vitreoretinal and Ophthalmic Surgeon performed all the procedures and followed up the patients on regular basis. Institutional ethical approval was acquired for this research and tenets of Declaration of Helsinki, applied.

Inclusion criteria: Patients in the study were those who were examined and diagnosed at the retina clinic of 37 Military Hospital in Accra, Ghana. Exclusion criteria were other co-morbidities in the affected eye: age related macular degeneration, macular hole, end stage glaucoma, retinitis pigmentosa, history of retinal detachment surgery and trauma. Out of 67 patients

whose medical records were reviewed, 27 were excluded from the study because they were either followed up for less than 5years or lost to follow up.

Some of the patients had been referred from other Sub-Saharan African countries. In addition to general demographic data, information on underlying systemic diseases, visual acuity, indication for procedures and latest Best Corrected Visual Acuity (BCVA) was collected and analyzed.

One Consultant Vitreoretinal and Ophthalmic Surgeon (FKO) did comprehensive eye examination at the Out-Patient Department to diagnose CRAO (fig 2 and 3). Those whose intra-ocular pressures were high (between 22 and 25mmHg) were given selective alpha-2 adrenergic receptor agonist (alphagan-P bd) and or carbonic anhydrase inhibitors (diamox 250 mg od). Other staff assisted in checking the patients's blood pressures, fasting or random blood sugar, fasting lipid profile and weight with the aim to identifying systemic risk factors. All patients were referred to the medical department emergency unit (MDEU) for further assessment, detection and management of systemic risk factors.

Physician specialists at MDEU, on the other hand, referred patients with underlying systemic diseases to the retina clinic for further evaluation especially if the latter complained of visual impairment. Some of these patients were on nasal oxygen therapy (NOT) and other medications (table 2) on account of acute ischaemic heart dsease and myocardial infarction. Another group of patients were on sublingual isosorbide dinitrate (Canadian brand Dilatrate-SR 5mg daily) due to angina from coronary artery disease. Another group of patients were on oral anticoagulation therapy (XARELTO, rivaroxaban) on account of atrial fibrillation (20mg daily), pulmonary embolism (15mg twice daily for 3 weeks, then 20mg daily) and deep vein thrombosis (10mg daily). Those with hypercholesterolaemia were managed with oral atorvastatin (VIATRIS LIPITOR10-80mg daily). Patients who had diabetes were on metformin (oral glucophage 1g to 3g daily). All clients who had hypertension were put on oral captopril (US brand capoten 25-450mg daily).

Snellen BCVA was converted into logarithm of minimum angle of resolution (logMAR) units in order to get better statistical analysis. Patients whose visual acuities were hand movement were assigned equivalence of 1.7 logMAR units.

III. Statistical Analysis

For normally distributed variables, paired t-test was used. All tests were considered statistically significant if p-value was 0.05 or less. Chi square test and paired t-test with SPSS and Graph Pad software were used respectively as shown in table 1.

IV. Results

Although all the patients had underlying systemic diseases, only 24 (60%) knew they had a chronic disease before the onset of CRAO. A total of 40 eyes of 40 patients (15 females and 25 males) were identified. Mean age at diagnosis was 70.4 + 3.5 (range 68-75 years) with minimum follow up period of 5 years (range 5 – 8).

Pre- and post-treatment BCVA which was generally hand motion did not change from the onset of CRAO until last follow up visit. Mean pre-treatment BCVA was 2.40+ 2.00logMAR units which depended on stage and severity of disease. The mean difference between final post- and pre-treatment visual acuity was 0.00±2.00 log MAR units which was statistically significant ($p < 0.005$).

Table 1: Shows statistical analysis

Syntax		T-TEST /TESTVAL=40 /MISSING=ANALYSIS /VARIABLES=PRETREATMENT POSTTREATMENT /CRITERIA=CI(.95).
Resources	Processor Time	00:00:00.00
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One-SampleStatistics

	N	Mean	Std. Deviation	Std. ErrorMean
PRE-TREATMENT	40	.00425	.002362	.000373
POST-TREATMENT	40	.00425	.002362	.000373

One-Sample Test

	Test Value = 40					
	T	Df	Sig. (2-tailed)	MeanDifference	95% Confidence Interval of the Difference Lower	
PRE-TREATMENT	-107114.068	39	.000	-39.995750	-39.99651	
POST-TREATMENT	-107114.068	39	.000	-39.995750	-39.99651	

In all 40 eyes were managed for CRAO with the most common aetiologies being hypertension (24;60%), hypercholesterolaemia (5;12.5%) and diabetes(5;12.5%) [table-2]. The most common causes of mortality were hypertension induced myocardial infarction (5;12.5%), pulmonary embolism (3;7.5%) and hypertension induced atrial fibrillation (1;2.5%). The use of isosorbide dinitrate, nasal oxygen therapy (NOT), anticoagulation and reduction in intraocular pressure was not able to improve visual acuities in the affected eyes. However, they played important role in prevention of some deaths and preserved vision in affected or contralateral better eyeas shown in table 2.

Table 2: CRAO Management Plan Summary

SRL	*Underlying Systemic Disease*	*Additional Eye Disease Apart from CRAO*	*Number of patient*	*Number of Eyes N (%)*	*Systemic Intervention*	*Primary Ocular Therapy*	*Mortality N (%)*
1	HPT and Angina	Nil	10	10 (25%)	Captopril and ISDN	Nil	0(0%)
2	Isolated HPT	Nil	7	7(17.5%)	Captopril	Nil	0(0%)
3	Hypercholesterolaemia	Nil	5	5 (12.5%)	Atorvastatin	Nil	0(0%)
4	Diabetes Mellitus	Ocular Hypertension	5	5 (12.5%)	Metformin	Diamox and alphagan-P	0(0%)
5	HPT and Myocardial Infarction	Nil	5	5 (12.5%)	Captopril and nasal oxygen therapy	Nil	5 (12.5%)
6	Pulmonary Embolism	Nil	3	3 (7.5%)	Anti-coagulation	Nil	3 (7.5%)
7	HPT and Atrial Fibrillation	Nil	1	1 (2.5%)	Captopril and Anti-coagulation	Nil	1 (2.5%)
8	DVT	Nil	3	3 (7.5%)	Anti-coagulation	Nil	0(0%)
9	HPT and IHD	Nil	1	1 (2.5%)	Captopril and nasal oxygen	Nil	1 (2.5%)

HPT- hypertension; DVT- Deep Vein Thrombosis; IHD- Ischaemic Heart Disease; ISDN- Isosorbide Dinitrate

V. Discussion

The idea behind ocular massage is to create fluctuations in intraocular pressure with intermittent retina arteriolar dilatation resulting in mechanical disintegration of the clot and reperfusion[23]. Although use of ocular massage to treat CRAO started in 1880, no study has demonstrated and established its efficacy. It has therefore been relegated to the background in modern literature since there is no scientific evidence to support its use. In the study hospital, the first two eyes which were massaged became hypotensive with corneal oedema. Subsequently, no other eye was subjected to massaging.

Hyperbaric oxygen therapy (HBOT) is used as a means of protecting retinal tissue in acute CRAO from severe ischaemia. Physiologically, choroidal circulation nourishes the retina with 50% of its oxygenneeds [24], a concentration which increases up to 97% with the use of HBOT [25]. A lot of scientific researchers have arrived at the conclusion that HBOT enhances visual recovery in the acute phase of CRAO [26,27,28] without necessarily re-establishing reperfusion of the retina permanently. Accordingly, another study published by Rozenberg et al substantiated the fact that HBOT improves visual

acuity significantly even 9 hours after CRAO [29]. Luca Rosignoli et al, however, have categorically established through their research that HBOT does not improve visual acuity [30]. Additionally, they realized its use is marred by complications like barotrauma, ear pain, tympanic membrane rupture, and generalized seizures due to oxygen toxicity of the central nervous system [30]. As the study hospital lacks HBOT, 6 patients with 6 eyes were subjected to nasal oxygen therapy due to underlying diseases like myocardial infarction (MI) and Ischaemic Heart Disease (IHD) as soon as the events occurred. There was no improvement of their visual acuities.

Carbogen is made up of 5% carbon dioxide (CO2) and 95% oxygen. The theory behind its use in CRAO management is that CO2 dilates the central retinal artery paving the way for passage of oxygen to nourish the retina [31,32]. Its practical use, however, is characterized by contradictions and poor outcomes [33,34]. In the study hospital, this therapy was not applied because it was not available.

Other researchers reduced intraocular pressure (IOP) pharmacologically even if it was normal to restore sight in CRAO but were not successful [35]. In the study hospital, 5 eyes in 5 patients were managed with carbonic anhydrase inhibitors (diamox) and a-2 selective adrenergic receptor agonist (alphagan) due to high IOP. None of the patients had improvement of their visual acuities.

Isosorbide dinitrate (ISDN) helps in generation of nitric oxide and contributes to dilation of choroidal, retinal and optic nerve vessels. Based on this theory, it has been used in combination with other therapies to re-establish retinal blood flow in CRAO [36]. In the study hospital, none of the 10 patients with 10 eyes who were treated with ISDN on account of angina had improvement of their visual acuities.

According to Cochrane review, there is no conservative treatment combined or monotherapy which is superior to placebo in management of CRAO [10,37]. In an attempt to get better results, researchers recruited 419 patients in 8 different studies which disappointedly gave poorer outcomes than the Cochrane study [38]. Accordingly, the American Academy of Ophthalmology recently conducted research concluding that conservative therapies play no role in the management of CRAO [39].

FieB A et al, in their study, established that anterior chamber paracentesis did not contribute to gaining of visual acuity regardless of interval between onset of symptoms and time of treatment [11]. Opremcak E et al also published a study in which lysis of emboli was achieved with YAG laser embolectomy. However, this procedure was marred by complications like vitreous haemorrhage and pseudoaneurysms making the whole procedure unreliable [12]. Similarly, a research conducted by Lu N et al revealed that pars plana vitrectomy with direct massage of the central retinal artery does not yield good results [13].In the study hospital, none of the above invasive therapies was used since they did more harm than good.

Intra-arterial thrombolysis (IAT) within 4.5 hours of occurrence of CRAO gained some good results [40,41,42,43]. Other studies, however, have shown poor results [44,45]. The NINDS trial [46], which involved 291 participants, found symptomatic intracranial haemorrhage within 36 hrs of treatment in 8% of the thrombolysis treatment group of which 4% was fatal compared with no events in the control group. Moreover, 3% of patients in the treatment group developed asymptomatic intracranial haemorrhage within 36 hrs of treatment and another 3% of the treatment group developed symptomatic intracranial haemorrhage on long-term follow-up. Since there was no IAT facility in the study hospital, pharmacological thrombolysis was made in 7 patients with 7 eyes who had anticoagulation on account of pulmonary embolism, deep vein thrombosis and atrial fibrillation within 4 hours of onset of the disease. None of them had improvement of their visual acuities. Thrombolysis (pharmacological or IAT) is therefore not a reliable modality of management.

Since there is no known established treatment for CRAO, it is therefore mandatory to re-channel its management towards secondary prevention: prevent mortality from peripheral vascular, cardiovascular and cerebrovascular diseases, avoid blindness in the affected eye and stop similar visual impairment occurring in the better eye. Prophylaxis can only be achieved if the underlying risk factors are detected and modified early enough [7]. In the study hospital, 25% (n=10) of patients died from several causes the most common of which was hypertension with myocardial infarction as shown in table 2.

VI. Limitation

Limitations of this study include its retrospective nature, single-centre focus, variable follow up lengths, and the fact that one retina specialist performed all procedures. Moreover, invasive therapies were not utilized due to lack of equipment or fear of worsening the patients' already poor sight.

VII. Conclusion and Future Therapeutic Approach

Ischaemic cerebrovascular accidents, myocardial infarction and CRAO have similar pathogenesis and therapeutic interventions. Although many ophthalmologists have diverse ways of managing CRAO, the fact remains that currently there is no conventionally accepted treatment modality substantiated by scientific evidence. Treatment dilemma is made worse by the fact that the retina, which is

extension of the brain and central nervous system, does not recover from ischaemic injuries because it lacks Schwann cells. Similarly, several comparative studies, as indicated above, have repeatedly established that no therapeutic intervention is superior to placebo or observation. Management of underlying risk factors equally plays a pivotal role as a preventive measure against blindness in same eye, visual impairment in the contralateral eye and death. A multidisciplinary team made up of ophthalmologists, physician specialists, family physicians and neurologists should be formed in all institutions to help in CRAO management.

Future therapeutic approaches should delve into how to revive the retina after CRAO has occurred. The success of such a study will lead to visual recovery, reversal of ischaemic stroke and good prognosis for myocardial infarction.

Bibliography

1. Leavitt JA et al. Am J Ophthalmol. 2011;152(5): 820-823
2. Hayreh SS, Zimmerman MB. Central retinal artery occlusion: visual outcome. Am J Ophthalmol2005; 140: 376.e1–376.e.
3. Park SJ, Choi N-K, Seo KH, et al. Nationwide incidence of clinically diagnosed central retinal artery occlusion in Korea, 2008 to 2011. Ophthalmology 2014; 121: 1933–8.
4. Leavitt JA, Larson TA, Hodge DO, Gullerud RE. The incidence of central retinal artery occlusion in Olmsted County, Minnesota. Am J Ophthalmol. 2011 Nov. 152 (5): 820-3.e2. [QxMD MEDLINE Link].
5. Lavin P, Patrylo M, Hollar M, Espaillat KB, Kirshner H, Schrag M. Stroke risk and risk factors in patients with central retinal artery occlusion. Am J Ophthalmol. 2019; 200: 271–272. doi: 10.1016/j.ajo.2019.01.021
6. Hayreh SS, Podhajsky PA, Zimmerman MB. Retinal artery occlusion: associated systemic and ophthalmic abnormalities. Ophthalmology. 2009; 116: 1928–1936. doi: 10.1016/j.ophtha.2009.03.006
7. Callizo J, Feltgen N, Pantenburg S, Wolf A, Neubauer AS, Jurklies B, Wachter R, Schmoor C, Schumacher M, Junker B, et al; European Assessment Group for Lysis in the Eye. Cardiovascular risk factors in central retinal artery occlusion: results of a prospective and standardized medical examination. Ophthalmology. 2015; 122: 1881–1888. doi: 10.1016/j.ophtha.2015.05.044
8. https://www.ncbi.nlm.nih.gov/books/NBK470354/#:~:text=An%20embolism%20is%20the%20most,typically%20arise%20from%20cardiac%20valves.
9. https://www.pulmonologyadvisor.com/home/decision-support-in-medicine/pulmonary-medicine/nonthrombotic-pulmonary-embolism-air-amniotic-fluid-fat-tumor/
10. Sim S, Ting DSW. Diagnosis and Management of Central Retinal Artery Occlusion. EyeNet Magazine. August 2017. [Full Text].
11. Fieß A, Cal Ö, Kehrein S, Halstenberg S, Frisch I, Steinhorst UH. Anterior chamber paracentesis after central retinal artery occlusion: a tenable therapy?. BMC Ophthalmol. 2014 Mar 10. 14:28. [QxMD MEDLINE Link].
12. Opremcak E, Rehmar AJ, Ridenour CD, Borkowski LM, Kelley JK. Restoration of retinal blood flow via translumenal Nd: YAGembolysis/embolectomy (TYL/E) for central and branch retinal artery occlusion. Retina. 2008 Feb. 28 (2): 226-35. [QxMD MEDLINE Link].
13. Lu N, Wang NL, Wang GL, Li XW, Wang Y. Vitreous surgery with direct central retinal artery massage for central retinal artery occlusion. Eye (Lond). 2009 Apr. 23 (4): 867-72. [QxMD MEDLINE Link].
14. Pielen A, Pantenburg S, Schmoor C, Schumacher M, Feltgen N, Junker B, et al. Predictors of prognosis and treatment outcome in central retinal artery occlusion: local intra-arterial fibrinolysis vs. conservative treatment. Neuroradiology. 2015 Oct. 57 (10):1055-62. [QxMD MEDLINE Link].
15. https://www.ncbi.nlm.nih.gov/books/NBK10885/#:~:text=Despite%20its%20peripheral%20location%2C%20the,%3B%20see%20also%20Chapter%2022).
16. Cugati S, Varma DD, Chen CS, Lee AW. Treatment options for central retinal artery occlusion. Curr Treat Options Neurol. 2013 Feb. 15 (1):63-77. [QxMD MEDLINE Link].
17. Shinozuka K, Dailey T, Tajiri N, Ishikawa H, Kim DW, Pabon M: Stem cells for neurovascular repair in stroke. J Stem Cell Res Ther. 2013, 4: 12912-
18. Chen C, Wang Y, Yang GY: Stem cell-mediated gene delivering for the treatment of cerebral ischemia: progress and prospectives. Curr Drug Targets. 2013, 14: 81-89. 2174/13894501380480 6497.
19. Wang X, Rosell A, Lo EH: Targeting extracellular matrix proteolysis for hemorrhagic complications of tPA stroke therapy. CNS Neurol Disord Drug Targets. 2008, 7: 235-242. 10.2174/1871527087849 36635.
20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC381398/
21. Hayreh SS. Acute retinal arterial occlusive disorders. Prog Retin Eye Res. 2011; 30: 359–394. crossrefpmidpmc
22. Angeli O, Nagy ZZ & Schneider M: Spontaneous visual recovery following a central retinal artery occlusion in a patient with a cilioretinal artery. Orv Hetil 2019, 160: 1146–1152. CrossrefPubMedWeb of Science®Google Scholar

23. Ffytche T. A rationalization of treatment of central retinal artery occlusion. Trans Ophthalmol Soc U K. 1974; 94: 468–79.
24. Landers MB 3rd. Retinal oxygenation via the choroidal circulation. Trans Am Ophthalmol Soc. 1978; 76: 528–556.
25. Dollery CT, Bulpitt CJ, Kohner EM. Oxygen supply to the retina from the retinal and choroidal circulations at normal and increased arterial oxygen tensions. Invest Ophthalmol. 1969; 8: 588–594
26. Bagli BS, Çevik SG, Çevik MT. Effect of hyperbaric oxygen treatment in central retinal artery occlusion. Undersea Hyperb Med. 2018;45: 421–425.
27. Lopes AS, Basto R, Henriques S, Colaço L, Costa E Silva F, Prieto I, Guerreiro F. Hyperbaric oxygen therapy in retinal arterial occlusion: epidemiology, clinical approach, and visual outcomes. Case Rep Ophthalmol Med. 2019;2019:9765938. doi: 10.1155/2019/9765938
28. Masters TC, Westgard BC, Hendriksen SM, Decanini A, Abel AS, Logue CJ, Walter JW, Linduska J, Engel KC. Case series of hyperbaric oxygen therapy for central retinal artery occlusion [published online July 10, 2019]. Retin Cases Brief Rep. doi: 10.1097/ICB.0000000000000895
29. Rozenberg A, Hadad A, Peled A, et al. Hyperbaric oxygen treatment for non-arteritic central retinal artery occlusion retrospective comparative analysis from two tertiary medical centres. Eye (Lond) 2021 Jun 17; doi: 10.1038/s41433-021-01617-8. [Epub]. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
30. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9013555/#:~:text=Large%2C%20randomized%20studies%20are%20required%20to%20better%20understand%20the%20role,the%20oxygen%20toxicity%20of%20the
31. Harino S, Grunwald JE, Petrig BJ, Riva CE. Rebreathing into a bag increases human retinal macular blood velocity. Br J Ophthalmol. 1995; 79: 380–3.
32. Arend O, Harris A, Martin BJ, Holin M, Wolf S. Retinal blood velocities during carbogen breathing using scanning laser ophthalmoscopy. Acta Ophthalmol. 1994; 72: 332–6.
33. Atebara NH, Brown GC, Cater J. Efficacy of anterior chamber paracentesis and Carbogen in treating acute nonarteritic central retinal artery occlusion. Ophthalmology. 1995; 102: 2029–34. discussion 2034–2025.
34. Deutsch TA, Read JS, Ernest JT, Goldstick TK. Effects of oxygen and carbon dioxide on the retinal vasculature in humans. Arch Ophthalmol. 1983; 101: 1278–80.
35. Fraser SG, Adams W. Interventions for acute non-arteritic central retinal artery occlusion. Cochrane Database Syst Rev. 2009; 2009: CD001989. doi: 10.1002/14651858.CD001989.pub2
36. Rumelt S, Dorenboim Y, Rehany U. Aggressive systematic treatment for central retinal artery occlusion. Am J Ophthalmol. 1999; 128: 733–8. [PubMed] [Google Scholar] [Ref list]
37. Fraser SG, Adams W. Interventions for acute non-arteritic central retinal artery occlusion. Cochrane Database Syst Rev. 2009: 1–14. [PMC free article] [PubMed] [Google Scholar] [Ref list]
38. Schrag M, Youn T, Schindler J, Kirshner H, Greer D. Intravenous fibrinolytic therapy in central retinal artery occlusion: A patient-level meta-analysis. JAMA Neurol. 2015; 72: 1148–54. [PubMed] [Google Scholar] [Ref list]
39. Flaxel CJ, Adelman RA, Bailey ST, Fawzi A, Lim JI, Vemulakonda GA, et al. Retinal and ophthalmic artery occlusions preferred practice pattern® Ophthalmology. 2020; 127: P259–87. [PubMed] [Google Scholar] [Ref list]
40. Mac Grory B, Nackenoff A, Poli S, Spitzer MS, Nedelmann M, Guillon B, Preterre C, Chen CS, Lee AW, Yaghi S, et al. intravenous fibrinolysis for central retinal artery occlusion: a cohort study and updated patientlevel meta-analysis. Stroke. 2020; 51: 2018–2025. doi: 10.1161/ STROKEAHA.119.028743
41. Préterre C, Godeneche G, Vandamme X, Ronzière T, Lamy M, Breuilly C, Urbanczyk C, Wolff V, Lebranchu P, Sevin-Allouet M, et al. Management of acute central retinal artery occlusion: Intravenous thrombolysis is feasible and safe. Int J Stroke. 2017; 12: 720–723. doi: 10.1177/1747493016687578
42. Nedelmann M, Graef M, Weinand F, Wassill KH, Kaps M, Lorenz B, Tanislav C. Retrobulbar spot sign predicts thrombolytic treatment effects and etiology in central retinal artery occlusion. Stroke. 2015; 46: 2322–2324. doi: 10.1161/STROKEAHA.115.009839
43. Schultheiss M, Härtig F, Spitzer MS, Feltgen N, Spitzer B, Hüsing J, Rupp A, Ziemann U, Bartz-Schmidt KU, Poli S. Intravenous thrombolysis in acute central retinal artery occlusion: a prospective interventional case series. PLoS One. 2018; 13:e0198114. doi: 10.1371/journal.pone.0198114
44. harma RA, Newman NJ, Biousse V. New concepts on acute ocular ischemia. CurrOpin Neurol. 2019; 32: 19–24. [PubMed] [Google Scholar] [Ref list]
45. Mac Grory B, Lavin P, Kirshner H, Schrag M. Thrombolytic therapy for acute central retinal artery occlusion. Stroke. 2020; 51: 687–95. [PubMed] [Google Scholar] [Ref list]
46. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995; 333(24): 1581–1587. doi: 10.1056/NEJM199512143332401 [PubMed] [CrossRef] [Google Scholar] [Ref list]

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Intraoperative Determination of the Actual Length of the Small and Large Intestine and its Relation to Anthropometric Variables in the Egyptian Population

By Mohamed Elshal

Abstract- *Background:* The primary function of small bowel is digestion and absorption of dietary components after they leave the stomach. The enlarged surface area of small intestine enables complete digestion of food stuffs. Investigators has correlated the length of small bowel with age, gender, height, and weight.

The aim of study: To asses intraoperatively the small bowel length measurements and analysis of demographic predictors of increased length.

Patients and methods: This cross-sectional study was conducted in Emergency Department of Cairo University hospital from January 2021 to June 2021.We included 160 patients who have been admitted to general surgery department of KasrAlainy who were indicated for abdominal surgery. Measurement the of the small bowel is expressed in centimeters, starting at ligament of Treitz and ending at the ileocecal junction using a sterile 10 cm- tape applied to the anti-mesenteric border of un stretched small intestine.

Keywords: *bowel, anthropometric variables, total small bowel length (TSBL), egyptian population.*

GJMR-I Classification: *NLMC Code: WI/QS*

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Results: The current study showed that there was very high positive correlation according to weight and height while BMI shows no significant correlation between them. We also found that there were highly statistically significant differences between sex groups according to age, height, BMI and Total small bowel length. In males, there was very high positive significant correlation according to weight and height. In females, there was very high positive significant correlation according to height.

Conclusion: Length of the small bowel in humans is pertinent to advances in deep enteroscopy and existing surgical applications such as intestinal bypass and prevention of short gut syndrome.

Keywords: bowel, anthropometric variables, total small bowel length (TSBL), egyptian population.

I. Introduction

The length of the small intestine varies from 3 to 8.5 meters. The average length is considered to be approximately 5 meters(1).

The variation in the intestinal length in humans is a topic of interest. Differences in measurement techniques, small study groups, and large inter-individual variation have contributed to the uncertainty associated with defining a normal range of intestinal length. Estimation of small bowel length is relevant for many years to plan small bowel resections as the development of malabsorption is closely related to the total length of small intestine that remains after surgery (2,3).

Measurement of small bowel length is relevant in planning bariatric surgery because the efficacy and incidence of malnutrition are closely associated with the length of the bilio-pancreatic (BP) limb, the common channel, and the total length of the small bowel. This advancement in knowledge regarding bariatric surgery has generated renewed interest in the importance of the length of the small bowel in this patient population(4,5).

Despite its great importance in surgical approaches, little definitive information is available on human gut tract length in Egyptian population. Previous studies have correlated small bowel length with various measures like sex, age, weight, height and ethnic background. Better knowledge of these relationships may aid in avoidance of surgical complications (6).

Prediction of the total small bowel length (TSBL) could be useful to avoid intraoperative measurements, which might consume extra time particularly in laparoscopic procedures in morbidly obese individuals. A CT scan–based prediction method has been proposed in the literature but without validation. There is significant controversy on the role of anthropometry as predictive parameters to the total small bowel length(TSBL)(7,8).

II. Patients and Methods

We conducted a prospective cross section study that included 160 patients (100 males, 60 females) presented to KasrAlainy hospital with indication for open abdominal exploration.

a) Inclusion criteria

Adult Patients aged ≥ 18 years, presenting with indication for open abdominal exploration such as blunt or penetrating abdominal trauma, Incarcerated or strangulated para umbilical hernia.

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b) Exclusion criteria

Patients aged less than 18 years. Patients presented with gastrointestinal tract malignancy. Patients presented with Peritonitis. Patients with history of Previous abdominal operation to avoid intestinal adhesions which may affect the proper measurement of the small bowel length.

Study procedures: All Patients enrolled in our study were be assessed on admission:-

History Taking, hemodynamic assessment, general and abdominal examination.

Imaging: X ray (chest erect and abdomen), ultra sound and CT.

Laboratory investigations: CBC, Na, k, urea, creatinine, ALT, AST, RBS and HbA1C.

Unstable cases such us abdominal stab with eviscerated bowel or Full from height will be rushed to the Operating room.

Intraoperative findings: Measurement the of the small bowel was expressed in centimeters, starting at ligament of Treitz and ending at the ileocecal junction, using a sterile 10 cm- tape applied to the anti-mesenteric border of un stretched small intestine.

Spasmolytic (visceralgine 5 mg/2 ml IV) was taken on induction of anesthesia to reduce the contractions of the small bowel.

All measurements were obtained by 2 trained surgeons to increase the accuracy of measurement.

III. Results

The study included 60 females and 100 males representing 37.7% and 62.3 %, respectively, of the study population. The mean age was 46.34±16.022 years, weight = 80.49±8.302 kg, height = 170.13±9.150 cm, and BMI = 28.02±4.112 kg/m2. The measurement of the TSBL in the study participants yielded a mean of 412.62±54.938 cm ranging from 310 to 560 cm as shown in Table (1).

Table (1): Descriptive statistics of the quantitative baseline variables assessed for this study

	Number	Percent
Age (years)		
Range	18-80	
Mean±S.D.	46.34±16.022	
Sex		
Male	100	62.5
Female	60	37.5
Weight		
Range	63-110	
Mean±S.D.	80.49±8.302	
Height		
Range	150-189	
Mean±S.D.	170.13±9.150	
BMI		
Range	20-43	
Mean±S.D.	28.02±4.112	
TSBL		
Range	310-560	
Mean±S.D.	412.62±54.938	

a) Causes of admission

Patient admitted were mainly due to stab abdomen 32 patients (20%), Incarcerated Para umbilical hernia 21 patients (13.12%), Road Traffic Accident 19 patients (11.87%), Fall from height 18 patients (11.25%) , Incarcerated inguinal hernia 12 patients (7.5%), Mesenteric Vascular Occlusion 10 patients (6.25%) *as shown in Table (2).*

Table (2): Causes of admission among the included patients

		Count	Percent
Cause of admission (n%)	Stab abdomen	32	20%
	Incarcerated Para umbilical hernia	21	13.12%
	Road Traffic Accident (RTA)	19	11.87%
	Fall from height (FFH)	18	11.25%
	Incarcerated inguinal hernia	12	7.5%
	Strangulated inguinal hernia	12	7.5%

	Mesenteric Vascular Occlusion (MVO)	10	6.25%
	Complicated appendicitis	10	6.25%
	Open cholecystectomy	8	5%
	Diverticulosis	6	3.75%
	Gall stone ileus	2	1.25%
	Bowel injury postoperative	2	1.25%
	Intestinal obstruction due to Fecolith	2	1.25%
	Ogilvie syndrome	2	1.25%
	Bowel injury post ERCP	2	1.25%
	Biliary leakage	2	1.25%

Table (3) shows that correlation between total small bowel length (TSBL) and the measured variables in the study and it show that there was very high positive correlation according to weight and height while BMI shows no significant correlation between them.

Table (3): Correlation between TSBL and the measured variables in the study

	TSBL			
	Pearson's		Spearman's rho	
	r	P	R	P
Age (years)	-0.047	0.557	-0.062	0.432
Weight	0.231	0.003*	0.212	0.007*
Height	0.455	<0.001*	0.434	<0.001*
BMI	-0.163	0.040*	-0.168	0.034*

Table (4): Comparison between gender groups according to baseline variables assessed for this study

	Gender		U	P value
	Female	Male		
Age				
Range	19 – 80	18 – 75	1987.00	<0.001*
Mean±S.D.	52.18±16.205	42.84±14.924		
Weight				
Range	65 – 110	63 – 105	2818.50	0.521
Mean±S.D.	79.93±8.8.578	80.83±8.156		
Height				
Range	150 – 189	150 – 189	739.50	<0.001*
Mean±S.D.	162.98±7.240	174.42±7.327		
BMI				
Range	21 – 43	20 – 41	1464	<0.001*
Mean±S.D.	30.17±3.962	26.74±3.653		
TSPL				
Range	310 – 560	330 – 560	2032.50	0.001*
Mean±S.D.	394.00±52.889	423.80±53.329		

Table (4) shows that comparison between gender groups according to baseline variables assessed for this study and it show highly statistically significant differences between sex groups according to age, height, BMI and total small bowel length (TSBL).

Table (5): Correlation between total small bowel length (TSBL) and the measured variables in male

	TSBL			
	Pearson's		Spearman's rho	
	r	P	R	P
Age (years)	0.087	0.390	0.097	0.339
Weight	0.270	0.007*	0.229	0.022*
Height	0.337	0.001*	0.311	0.002*
BMI	-0.012	0.906	0.012	0.907

Table (5) shows correlation between total small bowel length(TSBL) and the measured variables in male and it shows that there was very high positive significant correlation according to weight and height.

Table (6): Correlation between total small bowel length(TSBL) and the measured variables in female

	Total small bowel length(TSBL)			
	Pearson's		Spearman's rho	
	r	P	R	P
Age (years)	-0.058	0.658	-0.098	0.339
Weight	0.153	0.242	0.196	0.134
Height	0.468	<0.001*	0.486	<0.001*
BMI	-0.145	0.270	-0.109	0.406

Table (6) shows correlation between total small bowel length (TSBL) and the measured variables in female and it shows that there was very high positive significant correlation according to height.

IV. Discussion

Regarding the quantitative baseline variables assessed for this study, our results showed that there were 60 females and 100 males representing 37.5% and 62.5 %, respectively, of the study population. The mean age was 46.34±16.022 years, weight = 80.49±8.302 kilograms, height = 170.13±9.150 centimeters. The measurement of the TSBL in the study participants yielded a mean of 412.62±54.938 cm ranging from 310 to 560 cm.

Compared this study to others, according to ethnic background. The current study was supported by *Bekheit et al. (9)* conducted on Egyptian population, reporting the normal total bowel length in living adult humans and correlation with the anthropometric parameters. This study included 606participants (380 females and 226 males). Their mean age was 39.8 ± years, the mean TSBL was 630 ± 175 cm ranging from 250 to 1300 cm.

Also, the study by *Almalki et al. (10)* conducted on Taiwanese patients, mean age was 38.6±12.0 years and BMI was 38.9±7.6. Small bowel length varied widely among patients (mean 739.8 + 115.7 cm, range 380–1050 cm). Compared to Egyptian population in our study ranging from 310 to 560 cm. It is possible that Asian people have longer small bowel length than people of other races.

As well the study by *Tacchino, et al.(11)* aimed to evaluate small bowel length (SBL). The study enrolled 443 Italian patients out of them 342 were females (78%). The mean age was 37.7±10.4 years, the mean SBL of 443 patients undergoing laparotomy was 690 ± 93.7 cm (range 350–1049 cm). also, greater than mean small bowel length in Egyptian population. Compared to our study, *Varut et al., (12)* aimed to Evaluate the length of small bowel (SB) in Thai patients, the study enrolled 48 patients. There were 27 men and 21 women, with an average age of 60 years (range 28-88). The average length of SB was 428±105 cm (range 169-745).

Also, *Raines et al., (13)* aimed to estimate of small bowel length. The study enrolled 91 French patients, with male/female ratio of 51/40, the mean BMI was 29.45 ± 8.38. Small bowel length was found to vary widely between individuals (average 998.52 cm, range 630–1510 cm).

Furthermore, *Teitelbaum et al. (14)* aimed to present a series of intraoperative SBL measurements taken in North American patients undergoing laparotomy. Specific attention is paid to analyzing potential patient-specific predictors of SBL. The study enrolled 240 patients. 127 patients were female (53%). The mean age was 55 (range 20–86) years, mean height was 169 (range 138–196) cm and mean weight was 77(range 41–175) kg. Mean SBL from the ligament of potential patient-specific predictors of SBL. The study

enrolled 240 patients. 127 patients were female (53%). The mean age was 55 (range 20–86) years, mean height was 169 (range 138–196) cm and mean weight was 77(range 41–175) kg. Mean SBL from the ligament of Treitz to ileocecal value was 506±105 (range 285–845) cm.

Compared to previous studies, our study predict that the Egyptian population has shorter mean small bowel length (SBL), 412.62±54.938 cm ranging from 310 to 560 cm. compared to other populations of different ethnic background. Regarding the correlation between total small bowel length(TSBL) and the measured variables in the study, we found that there was very high positive correlation according to weight and height while BMI shows no significant correlation between them.

The study by Bekheit et al. (9) reported that there was very weak (i.e., negligible) positive but statistically significant correlation between the total small bowel length (TSBL) and both weight and height. There was no significant correlation between the TSBL and BMI or the age on the other hand. This was partially agreed with our results.

Also, supporting our study, Almalki et al. (10) in linear regression analysis revealed a significant association between small bowel length and body height, body weight, and waist circumference, but not significantly correlated with age.

As well, Tacchino et al. (11) in multivariate linear regression analysis model to predict SBL reported that sex, age, height, and weight showed a significant correlation ($P < .00001$).

The study by Purandare et al. (15) reported that there was no significant correlation between BMI and TSBL.

In addition, Raines et al., (13) in a linear regression analysis demonstrated a statistically significant relationship between small bowel length and height (regression coefficient = 0.0561, P-value = 0.0238). A linear relationship between small bowel length and weight or BMI was not observed.

As well, Teitelbaum et al., (14) reported that height was positively associated with increased SBL ($P < 0.001$). A multivariate linear regression model using patient sex, age, height and weight was significant (P= 0.001) and the predictors explained 8% of the variance in SBL. In this model, only height was independently predictive of increased SBL (P = 0.03). This was partially agreed with our results.

Hosseinpour et al. (16) reported that there was no significant correlation between height and small intestinal length.

Comparison between gender groups according to baseline variables assessed for this study showed that there were highly statistically significant differences between sex groups according to age, height, BMI and TSBL. where TSBL was significally longer in males compared with females.

However, the study by Bekheit et al. (9) on the assessment of the gender influence on the various anthropometric measures and the total small bowel length (TSBL), reported that males had significantly higher weight and were significantly taller compared with females. There was no difference in the BMI or age between males and females. However, the total small bowel length (TSBL) was significantly longer in males compared with females. The mean TSBL in males was 661.5 ± 186 cm versus 612 ± 164 cm. they also noted that the correlation between TSBL and height is stronger in males than females but with no statistical difference. This comes in agreement with our study (17).

Also, in agreement with our results *Almalki et al. (10)* reported that there was statistically significant association between sex and small bowel length.

Similarly, the study by *Teitelbaum et al. (14)* reported that Male sex and height had positive correlations with SBL. In men, height had a positive association with SBL (r=0.20, P= 0.03), whereas in women there was no correlation between height and SBL (r = 0.06, P = 0.51). In men, age had a trend toward a positive correlation with SBL (r = 0.17, P = 0.08), whereas in women age was negatively correlated with SBL (r= 20.18, P = 0.04). A multivariate linear regression model using sex, age, height and weight to predict SBL was significant (P = 0.001) and explained 8% of the variance in SBL. Increased height was the only significant independent predictor of increased SBL (P = 0.03) in this model.

Similar results were reported by recent study conducted by *Hosseinpour and Behdad A. (16)* where mean intestinal length was longer in females (468 cm) than males (459 cm). On the contrary, studies conducted by *Nordgren et al. (18)* and *Teitelbaum et al. (14)* reported that males had longer intestinal length than females.

V. Conclusion

Length of the small bowel in humans is pertinent to advances in deep enteroscopy and existing surgical applications such as intestinal bypass and prevention of short gut syndrome. The current study showed that the mean total small bowel length (TSBL) in the studied cases was 412.62±54.938 cm ranging from 310 to 560 cm. Which was lower than average small bowel length (SBL) of other population of different ethnic background, the current study showed that there was very high positive correlation according to weight and height while BMI shows no significant correlation between them. We also found that there were highly statistically significant differences between sex groups according to age, height, BMI and TSBL. In males, there was very high positive significant correlation according

to weight and height. In females, there was very high positive significant correlation according to height.

References Références Referencias

1. *Minko E., Pagano A., Caceres N., Tony Adar T., Márquez S. (2014)* Human intestinal tract length and relationship with body height. FASEB J. 28: 916.4.
2. *Sonali A Khake, Maitreyee M Mutalik (2018).* Variability of small bowel length: Correlation with height, waist circumference, and gender Sonali. Italian Journal of Anatomy and Embryology,; Volume 123, Pages 312-319/
3. *Smyth G.B. (1988)* Effects of age, sex, and post mortem interval on intestinal lengths of horses during development. Equine Vet. J. 20: 104-108.
4. *Schiller, Lawrence R; Pardi, Darrell S; Spiller, Robin; Semrad, Carol E; Surawicz, Christina M; Giannella, Ralph A; Krejs,Guenter J; Farthing, Michael J G; Sellin, Joseph H (2014).* Gastro 2013 APDW/WCOG Shanghai Working Party Report: Chronic diarrhea: Definition, classification, diagnosis. Journal of Gastroenterology and Hepatology, 29(1), 625.
5. *Sinha R., Trivedi D., Murphy P.D., Fallis S. (2014)* Small intestinal length measurement on MR enterography: Comparison with in vivo surgical measurements. AJR Am. J. Roentgenol. 203: W274-W279.
6. *Quan V, Cooper FPM, Bekheit M (2017).* The influence of total bowel length on gastric bypass outcomes. Mini-Invasive Surg:958.
7. *Tiberi A, Pesi B, Giudici F, Zambonin D, Nelli T (2020),* Cupellini C, Ficari F, Cianchi F, Scaringi S. Laparoscopic ileo-colic resection and right hemicolectomy for Crohn's disease and colon cancer: a preliminary comparative study on post-operative outcome. Updates Surg. Sep; 72(3): 821-826.
8. *Tran T., Sundaram C.P., Bahler C.D., Eble J.N.(2015)* Grignon D.J., Monn M.F., Simper N.B., Cheng L. Correcting the shrinkage effects of formalin fixation and tissue processing for renal tumors: toward standardization of pathological reporting of tumor size. J. Cancer 6: 759-766.
9. *Bekheit M, Ibrahim MY, Tobar W, Galal I, Elward AS. Correlation (2020 Feb)* between the total small bowel length and anthropometric measures in living humans: cross-sectional study. Obesity Surgery.; 30(2): 681-6.
10. *Almalki OM, Soong TC, Lee WJ, Chen JC, Wu CC, Lee YC (2021 Jan).* Variation in Small Bowel Length and Its Influence on the Outcomes of Sleeve Gastrectomy. Obesity Surgery.; 31(1):36-42.
11. *Tacchino R.M. (2015)* Bowel length: measurement, predictors, and impact on bariatric and metabolic surgery. Surg. Obes. Relat. Dis. 11: 328-334.
12. *VarutLohsiriwat MD, Wiangphoem N, Lohsiriwat S (2014).* The length of small bowel in Thai patients. J Med Assoc Thai.;97(5):525-9.
13. *Raines D, Arbour A, Thompson HW, FigueroaBodine J, Joseph S. (2015 Jan);* Variation in small bowel length: factor in achieving total enteroscopy?. Digestive Endoscopy. 27(1):67-72.
14. *Teitelbaum EN, Vaziri K, Zettervall S, Amdur RL (2013 Oct),* Orkin BA. Intraoperative small bowel length measurements and analysis of demographic predictors of increased length. Clinical anatomy.; 26(7): 827-32.
15. *Purandare A, Phalgune D, Shah S. (2019 Oct);* Variability of length of small intestine in Indian population and its correlation with type 2 diabetes mellitus and obesity. Obesity Surgery. 29(10):3149-53.
16. *Hosseinpour M, Behdad A (2008).* Evaluation of small bowel measurement in alive patients. SurgRadiolAnat; 30:6435
17. *Hounnou G., Destrieux C., Desme J., Bertrand P., Velut S.(2002)* Anatomical study of the length of the human intestine. Surg. Radiol. Anat. 24: 290-294.
18. *Nordgren S, McPheeters G, Svaninger G. (1997)* Small bowel length in inflammatory bowel disease. Int J Color Dis.; 12: 2304.

Figures Legend

Fig (1): Pie chart showing gender distribution among the included patients.

Fig (2): Cause of admission (indication of surgery).

Fig (3): Correlation between TSBL and measured variables in the study.

Fig (4): Correlation between TSBL and the measured variables in male.

Fig (5): Correlation between TSBL and the measured variables in female.

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An Audit on the Role of Sentinel Lymph Node Biopsy (SLNB) in High Risk of Invasion DCIS and Encysted Papillary Carcinoma

By Mona Sulieman, Matthew Davies, Hamza Arabiyat, Hussein Ali, Ghadah Alyahya, Kali Potiszil, Imran Abbas, Iain Brown, Polly King, Rachel English & Philip Drew

Abstract- *Background:* The incidence of breast ductal Carcinoma in Situ (DCIS) has been increasing; it currently represents up to 20-25% of all breast carcinomas. Encysted papillary cancer (EPC) is a rare form of breast carcinoma previously compared to DCIS which has been shown to present histologically with invasion of the basement membrane and even metastasis.

Aims: Our objective was to define a 'high risk' group of patients with pre-op diagnosis of non-invasive cancer undergoing breast conserving surgery (BCS), who would then benefit from SLNB.

Methods: A retrospective data collection including all the patients with DCIS over the last 5 years was performed. High risk was defined as: Extensive micro-calcification >40mm or any mass forming DCIS. EPC patients were collected via a Winpath search.

Keywords: *ductal carcinoma in situ; sentinel lymph node biopsy; encysted papillary carcinoma.*

GJMR-I Classification: *NLM: WP*

Strictly as per the compliance and regulations of:

An Audit on the Role of Sentinel Lymph Node Biopsy (SLNB) in High Risk of Invasion DCIS and Encysted Papillary Carcinoma

Mona Sulieman [α], Matthew Davies [σ], Hamza Arabiyat [ρ], Hussein Ali [ω], Ghadah Alyahya [¥], Kali Potiszil [§], Imran Abbas [χ], Iain Brown [ν], Polly King [Θ], Rachel English [ζ] & Philip Drew [£]

Abstract- ***Background:*** The incidence of breast ductal Carcinoma in Situ (DCIS) has been increasing; it currently represents up to 20-25% of all breast carcinomas. Encysted papillary cancer (EPC) is a rare form of breast carcinoma previously compared to DCIS which has been shown to present histologically with invasion of the basement membrane and even metastasis.

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Methods: A retrospective data collection including all the patients with DCIS over the last 5 years was performed. High risk was defined as: Extensive micro-calcification >40mm or any mass forming DCIS. EPC patients were collected via a Winpath search.

Results: 188 DCIS patients were deemed high risk due to >40mm calcification or a mass forming (radiological or palpable), 61% of those had a mastectomy and 32% underwent BCS and 85% had a SLNB. For the BCS patients, 42% had SLN at time of surgery and 13% (8 patients) at a second operation. Within the EPC patient group, the provisional diagnosis of encysted papillary carcinoma was upgraded to invasive carcinoma on final histology in around a third of cases.

Conclusions: We have defined a 'high risk' group of patients with a pre-op diagnosis of non-invasive cancer undergoing BCS, who would benefit from SLNB at the time of the surgery.

Keywords: ductal carcinoma in situ; sentinel lymph node biopsy; encysted papillary carcinoma.

I. Background

The incidence of breast ductal Carcinoma in Situ (DCIS) currently represents up to 20-25% of all breast carcinomas but its management remains controversial (1). In ductal carcinoma in situ of the breast (DCIS), histological diagnosis obtained before surgical treatment carries the risk of under staging the disease if the presence of invasive cancer is then found postoperatively. These patients need a second operation to assess the nodal status. Assessing the risk of under staging DCIS patients with even small lesions presenting as a mass would be helpful for optimal treatment planning. This should be considered in the decision-making process with regards to the extent of surgical intervention (2).

The overall natural progression of DCIS to invasive malignancy is reported to range from 14 to 75%. Histopathologic diagnosis of breast cancer should be obtained before the definitive treatment using minimal-invasive investigations. However, when invasive ductal cancer (IDC) is subsequently found in postoperative specimens these patients often need a further operation, usually a sentinel node biopsy to assess the nodal status.

Among the radiological features a mammographic extent of more than 4–5 cm and the presence of architectural distortion, focal asymmetric density or mass on mammography are proven important risk factors of final histological upstaging of DCIS to invasive carcinoma. In some reports, a mass lesion visible on ultrasound can be significantly related to the risk of upstaging DCIS to invasive ductal carcinoma. The cut-off points of lesion size that makes a distinction between low and high risk DCIS are still subjects of debate (3).

In the majority (62%–98%) of cases, DCIS is detected due to the presence of calcifications at mammography. In 2%–23% of cases, DCIS may manifest as a mass or asymmetry. The ultrasonographic (US) features of DCIS can be subtle and nonspecific however advances in US technology have improved the ability not only to characterize mammographic masses and asymmetries, but also to detect calcifications. Alongside increased implementation of US for screening and for targeted evaluation of breast magnetic resonance (MR) imaging abnormalities, recognizing the US features of DCIS has become increasingly important (4).

Encysted papillary cancer (EPC) is a rare form of breast cancer accounting for approximately (1–2%) of all breast tumors, usually presenting in postmenopausal women. The prediction of the biological behavior of this rare form of breast cancer and the clinical outcome is associated with an overall favorable prognosis;

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however, its consideration as a form of ductal carcinoma in situ with non-invasive nature is unclear as it has been shown to present histologically with invasion of basement membrane and even metastasis (5).

Both DCIS and encysted papillary carcinomas are pathologically non-invasive but clinically have a risk of metastasising to axillary lymph nodes, presumably due to a pathological sampling error. Therefore, offering sentinel lymph node biopsy (SLNB) to this pre invasive carcinomas category when performing breast conserving surgery is controversial. Initial SLNB should be considered for patients diagnosed with DCIS by needle biopsy when they have a high risk for harbouring invasive ductal cancer preoperatively (6). However, performing a sentinel lymph node biopsy also carries the risk of potentially unnecessary additional surgery with associated comorbidity.

II. Methods

The source of the data for the EPC was via a Winpath search from January 2014 to March 2019 using the term 'papillary carcinoma'. This produced 85 results, however from this a number of cases including micropapillary carcinoma and papilloma that were not EPC's were excluded. The results included two entries, one for the biopsy (EPC/B5a) and one for the subsequent excision. The search also found 3 cases of EPC on excision that initially were called papillary lesions/B3/B4. Additionally, 5 cases were excluded due to arising from background/neighbouring EPC's. In total 29 patients were identified to have EPC on biopsy.

The source of data for the DCIS again utilised a search on WinPath using the term 'DCIS' from January 2013 to April 2019 for all core biopsies including VABs. This generated a total of 637 patients of which any patients with invasive carcinoma or patients with a focus of invasion in the initial core biopsy were then excluded. This left 388 patients who were then inputted into an Excel spreadsheet. The following details were then included: referral route (screening, symptomatic or incidental), Clinical score (P score), Radiological score (R and U), imaging size (mm), presentation (mass forming DCIS or micro calcification only), high risk of occult invasion (mass forming or microcalcification of 40mm or more), date of surgery, details of surgery, excision diagnosis, final tumour size, SLNB performed, SLNB results. This data was collected from Maxims (hospital electronic patient record software).

III. Results

a) Encysted papillary carcinoma results

Of the 29 patients found to have EPC on core, 16 (55%) were found to be EPC on excision, while 9 (31%) were found to be invasive carcinoma on excision. A further 4 (14%) had no further surgery after the core (Table 1).

Table 1

EPC on core	EPC on excision	Invasive carcinoma on excision	No further surgery after core
29	16 (55%)	9 (31%)	4(14%)

From the EPC patient group, 72% of the patients were symptomatic on presentation while 28% were found on screening. Of those presenting all were female and their ages ranged between 51 and 91. The median age of presentation was 71.

Of the EPC patients, 5 (21%) underwent a mastectomy, 19 (65%) had a local wide excision and 4 (14%) underwent no surgery. Within the patient group undergoing no surgical intervention for EPC, 3 (75%) had PET and 1 (25%) had no treatment.

Within the EPC patient group, 5 of the patients underwent mastectomy of which all had SLNB at the time of operation as per protocol. Of the remaining 20 patients, 5 had SLNB at the time of operation, 5 (40%) had SLNB at a later stage and 10 never underwent SLNB. Of the SLN biopsies for EPC, 2 of the 15 (13%) who underwent SLNB were found to have positive nodes (Figure 1) Of those who had mastectomy, 2 of the 5 (40%) had positive nodes. Of those who underwent breast conserving surgery, none of the patients had positive nodes.

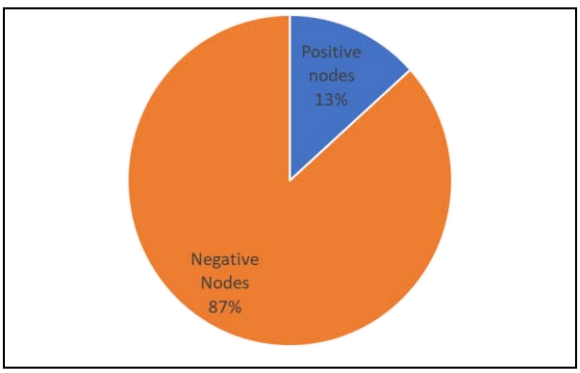

Figure 1: SLN results for EPC

b) DCIS data analysis

Of the 396 patients with DCIS, 188 (48%) were found to be high risk, while 206 (52%) were found to be low risk. Within this group the age range was between 33 and 83 with a mean age of 66, all of which were female. 130 (69%) of the high risk patient group were found from sampling, 50 (27%) were symptomatic and a further 8 (4%) were incidental.

Of the high-risk patients, 114 (61%) underwent mastectomy, 60 (32%) had BCS and 14 (7%) had no surgical intervention. 75 (40%) of the total high risk patients had a simple mastectomy, 39 (21%) had a mastectomy and immediate Recon, 36 (19%) had a WLE and 19 (20%) had a total mastectomy.

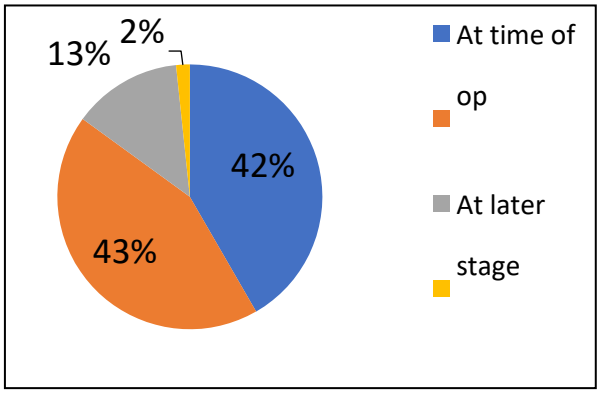

Figure 2: SLNB for high risk DCIS + BCS population

Within the patient group that underwent no surgical intervention, 6 (44%) received primary endocrine therapy (PET) either due to comorbidities or patient choice. Final excision histology for high risk DCIS (post operative) found that 38% were found to have invasive disease, whereas 13% of the low risk DCIS group were found to have invasive histology.

Within the high-risk DCIS group, 139 (80%) had a SLNB at the time of the operation and a further 8 (5%) had an SLNB later (Figure 4). Of the total high-risk patients (188) there were 114 who underwent mastectomy and thus had SNLB at the time of the operation. Of the 60 who had breast conserving surgery, 33 (55%) underwent SNLB either at the time of operation or at a later stage. This leaves however 26 patients (43%) who never received a SLNB (Figure 2).

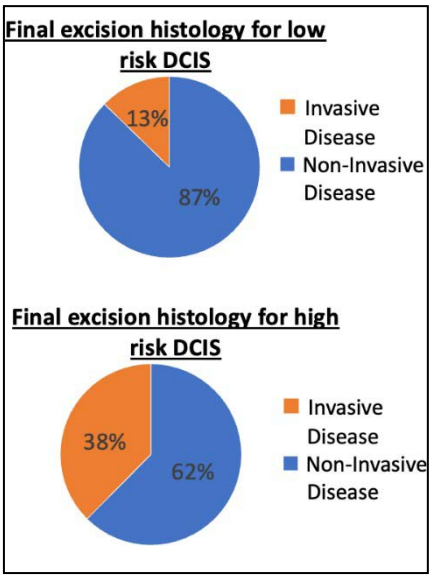

Figure 3: Post Histology results for DCIS groups

Of these patients, 23 of the 26 (87%) were found to have no invasive disease on final histology hence had no SLNB (Figure 3).

The results of the SNLB within the high-risk DCIS population revealed 15 patients had a positive SLNB which represents 7.9% of the entire high risk

patient population (Figure 3). Their age range was between 43 years to 81 years old (mean age 65 years). 9 patients presented symptomatic while a further 6 were screen detected. 11 patients were identified to have mass forming DCIS and 4 were found to have macrocalcification of more than 40mm on investigation. These high-risk DCIS patient groups surgical procedures consisted of: 11 mastectomies, 3 WLE and one TM. 14 of these patients had SLNB at time of initial operation whereas one patient had a subsequent SLNB. This single patient was 58 years old and initially diagnosed with 8mm mass forming DCIS on imaging and core biopsy. He was recorded as P1 R3 U4 and initially underwent WLE. This resulted in an excision diagnosis of G2 hence subsequent SLNB and positive results.

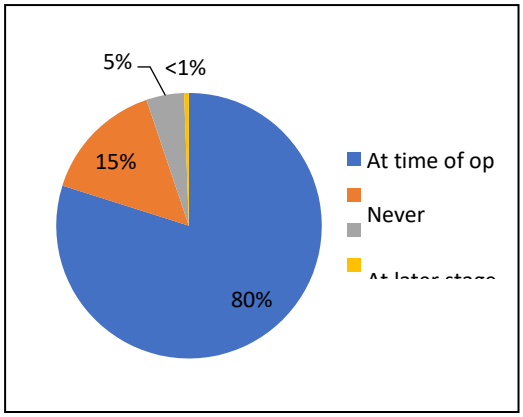

Figure 4: SLNB undertaken for high risk DCIS patient group

IV. Discussion

a) EPC Analysis

EPC analysis from the pathology department Audit we found that the provisional diagnosis of encysted papillary carcinoma was upgraded to an invasive carcinoma on final histology in around a third of cases. This has an implication for surgical planning with regards to SLNB offering at the time of surgery. According to our Audit data, the age of patients with EPC ranges from 51- 91year-old women, with a mean age of 72, which is a little older than the literature suggests and gave an older mean age for patients with DCIS. EPC is most commonly found in postmenopausal women (7). In our Audit data we found 72% were symptomatic and 28% were screen detected and this is in agreement with other published data. Encysted papillary carcinoma presents as a palpable lump in 70-80% of cases and then less commonly as nipple discharge or incidental finding (8). In our Audit analysis we found 70% were symptomatic with either lumps or nipple discharge. However, we found that nearly 30% presented via screening.

Treatment of EPC consists of surgery (wide local excision or mastectomy) ± radiotherapy (RT) ± hormonal treatment. The question of an axillary procedure remains unanswered with some series reporting the metastatic potential of EPC and recommending sentinel lymph node biopsy (SLNB) (7). Our data analysis showed that, the surgical treatments for this group were mostly BCS (65%), mastectomy (21%) and 14% had no surgery. The patients not undergoing surgery received primary endocrine treatment due to associated medical co-morbidities or had no active treatment as oestrogen/progesterone receptors were negative.

Patients with EPC require sentinel lymph node biopsy (SLNB) for staging of the axilla, only if there is evidence or suspicion of invasion in their core biopsy or final histology specimen or if they are undergoing a mastectomy as their primary treatment (9). When mastectomy was planned, SLNB's were offered to all 5 patients. Of the 20 patients who had BCS, 5 of them had a SLNB at the time of operation and another 5 had an SLNB at a later date (due to finding invasive components at final histology).

From these sentinel node biopsies, it was found that 87% were negative for nodal metastasis and 13% were positive for nodal metastasis. Of those undergoing BCS, 0 of the 9 patients had positive nodes.

b) DCIS analysis

According to the considered literatures we defined the high risk of invasion in this group as follows: Extensive micro-calcification >40mm, or any size mass forming DCIS. After applying this definition, we found that, 188 (48%) were high risk of invasion.

Within the group all were females, and their ages ranged from 33 to 88, with a mean age of 66. As expected, the majority were screen detected DCIS (69%), versus 27% symptomatic and only 4% were incidental at their presentation. We found that the surgical treatments in this group were mostly mastectomy in about 62% of cases including both simple mastectomies and immediate breast reconstruction. Breast conserving surgery made up

around 32%, including wide local excision, therapeutic mammoplasty, quadrantectomy and excision biopsies for diagnosis and proofed therapeutic treatment. Finally, around 7% had no surgical intervention, this because they had primary endocrine treatment for either co morbidity or patient's choice. On final post operative histology, we found, out of those who were classed as high-risk DCIS about 38% were found to have invasive disease on final histology. This compares to 13% of "low risk DCIS" that were found to have invasive disease on final histology.

According to the literature, initial SLNB should be considered for patients diagnosed with DCIS by needle biopsy when they have a high risk for harbouring invasive ductal cancer preoperatively (10). Patients in whom a preoperative diagnosis of DCIS is likely to be upgraded to invasive carcinoma will benefit from SLNB biopsy being performed with the initial surgery (11). Therefore, in these patients' group, we found 139 (80%) had SLNB at time of operation, 8 (5%) had SLNB at later stage, 26 (15%) never had a SLNB and 1 (less than 1%) declined the SLNB.

114 patients underwent mastectomy and had SLNB at time of operation as per protocol and guidelines. Of the 60 who had breast conserving surgery; 25 (42%) had SLNB at time of operation, 26 (43%) never had SLNB, 8 (13%) had SLNB at a later stage (all these patients were found to have invasive cancer on excision histology), only 1 patient (2%) declined the SLNB.

Despite a 23% upstaging rate, the rate of clinically significant positive SLNs in patients treated with BCS is low, supporting omission of upfront SLNB (30). Similarly, we found in our study that among the patients who had an axillary assessment, their histology results were mostly negative (92.1%), however of the patients with high- risk DCIS, 15 (7.9%) had a Positive SLNB. 11 out of these 15 patients had a mastectomy as their operation. This indicated a large DCIS size subset that necessitates a mastectomy. With the new technique of partial breast reconstruction SLNB should be offered in those cases to be able to predict the risk of invasion and even involved lymph node with metastatic carcinoma. Further analysis of the high- risk group, either extensive microcalcification or mass forming DCIS showed, of those 113 who had extensive microcalcifications 88 had SLN (78%) and 4 had positive nodes (4%). Of those 82 who had mass forming, 40 had SLN (49%) and 4 had positive nodes (4%). The total percentage of positive lymph nodes in these groups were about 8%. Regarding mass forming DCIS, we found 65% had SLNB and 35% didn't have SLNB, of those who had SLNB, 5% had positive nodes and just above 60% had negative nodes and 34% didn't have SLNB at all. Of the cohort that were screen detected masses, 33% had SLNB and of those 5% had a positive node. Additionally, patients who had high risk DCIS detected incidentally, 50% had SLNB and none had positive nodes histologically.

V. Conclusions

Within the encysted papillary carcinoma group the overall results showed that the provisional diagnosis of encysted papillary carcinoma is upgraded to an invasive carcinoma on final histology in around a third of cases. This may have an implication when deciding surgery and sentinel node biopsy should be offered at the time of therapeutic surgery. We should offer SLNB to patients with large sized EPC, which necessitate a mastectomy (tumour size is 40mm or above on imaging).

In terms of the risk of invasive ductal carcinoma in situ (DCIS), in this Audit, we have defined a 'high risk' group of patients with pre-op diagnosis of non-invasive cancer undergoing BCS, who would benefit from SLNB at the time of the surgery. These are those with extensive microcalcifications of more than 40 mm, or any size mass forming DCIS. When counselling patients within this group the risk of them having invasive disease in final histology is up to 40%, but the risk of sentinel node involvement is approximately 8%.

Recommendations

As a result of this audit, SLNB is offered at the time of initial surgery to the patients with high-risk DCIS and EPC to avoid further operations at later stage, which may result in increased patient emotional burden and higher service cost.

Audit Registration/Approval

Audit registration and Approval was obtained from Royal Cornwall Hospital, clinical effectiveness department.

Declarations of interest: None

References Références Referencias

1. Lissidini G, et al, Breast Ductal Carcinoma In Situ (DCIS): Open controversies and Guidelines Update of the European Institute of Oncology (EIO), Milan, European Journal of Surgical Oncology; Feb 2019; vol. 45 (no. 2).
2. Bartlomiej Szynglarewicz, et al, preoperatively diagnosed ductal cancers in situ of the breast presenting as even small masses are of high risk for the invasive cancer foci in postoperative specimen, World Journal of Surgical Oncology, July 2015, Article number: 218 (2015).
3. Leonard GD, Swain SM. Ductal carcinoma in-situ, complexities and challenges. J Natl Cancer Inst. 2004; 96:906–20.
4. Lilian C. Wang, Megan Sullivan, Hongyan Du, Marina I. Feldman, Ellen B. Mendelson, US Appearance of Ductal Carcinoma in Situ, Published

Online: Jan 1 2013 https://doi.org/10.1148/rg.331125092
5. Lissidini G, et al, Breast Ductal Carcinoma In Situ (DCIS): Open controversies and Guidelines Update of the European Institute of Oncology (EIO), Milan, European Journal of Surgical Oncology; Feb 2019; vol. 45 (no. 2).
6. Hotton, et al, Predictive factors of axillary positive sentinel lymph node biopsy in extended ductal carcinoma in situ treated by simple mastectomy at once, Journal of gynaecology obstetrics and human reproduction; Sep 2019; p. 101641.
7. Uemoto Y.; et al, Sentinel lymph node biopsy is unnecessary in ductal carcinoma in situ patients diagnosed by biopsy, Cancer Research; Feb 2019; vol. 79 (no. 4).
8. Nicole Nicosia Esposito, MD, David J. Dabbs, MD, Rohit Bhargava, MD, Are Encapsulated Papillary Carcinomas of the Breast In Situ or Invasive? A Basement Membrane Study of 27 Cases, American Journal of Clinical Pathology, Volume 131,
9. Price, Alison, et al, Sentinel lymph node positivity in patients undergoing mastectomies for ductal carcinoma in situ (DCIS), The breast journal; Jan 2020, Journal Article, PubMed: 31957944.
10. Pilewskie et al, Is Sentinel Lymph Node Biopsy Indicated at Completion Mastectomy for Ductal Carcinoma In Situ? Annals of surgical oncology; Jul 016; vol. 23 (no. 7); p. 2229-2234, PubMedID: 26960927
11. Andrea V. Barrio and Kimberly J. Van Zee, Controversies in the Treatment of DCIS, Annual Rev Med. 2017 Jan 14; 68: 197–211. doi: 10.1146/annurev-med- 050715-104920.

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Costs and Effects of Left Atrial Venous Drainage Cannula Placement in Veno-Arterial Extracorporeal Membrane Oxygenation (LAVA ECMO) Via Transeptal Puncture for Left Heart Decompression – A Single Institution Case Series

By Aurelie Merlo, MD, Panagiotis Tasoudis, MD, Lavinia Kolarczyk, MD, Joseph Rossi, MD, & Paul Tessmann, MD, PharmD

Abstract- *Background:* Peripherally cannulated patients on veno-arterial extra corporeal membrane oxygenation support may require left heart venting to offload the left ventricle and allow for myocardial rest and recovery. Which venting strategy is optimal is currently not known.

Methods: We performed a retrospective single-institution case series of fifteen patients who underwent left atrial venous drainage veno-arterial ECMO. The venous drainage cannula was a multistage single venous drainage cannula that was placed with fluoroscopic and echocardiographic guidance across the inter-atrial septum. The primary outcome of interest was six-month survival. Secondary outcomes included echocardiographic indices of left ventricular distention, platelet and bilirubin trend post cannulation, survival on ECMO, and surgical outcome.

Keywords: *ECMO, cardiogenic shock, myocardial recovery.*

GJMR-I Classification: *NLM: WG 500*

Strictly as per the compliance and regulations of:

Costs and Effects of Left Atrial Venous Drainage Cannula Placement in Veno-Arterial Extracorporeal Membrane Oxygenation (LAVA ECMO) Via Transeptal Puncture for Left Heart Decompression – A Single Institution Case Series

A Trial Decompression on VA ECMO

Aurelie Merlo, MD [α], Panagiotis Tasoudis, MD [σ], Lavinia Kolarczyk, MD [ρ], Joseph Rossi, MD [ω], & Paul Tessmann, MD, PharmD [¥]

Abstract- ***Background:*** Peripherally cannulated patients on veno-arterial extra corporeal membrane oxygenation support may require left heart venting to offload the left ventricle and allow for myocardial rest and recovery. Which venting strategy is optimal is currently not known.

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Results: Fifteen patients were cannulated using LAVA ECMO between January 2018 and June 2022. At six months, four patients were still alive. Echocardiographic assessment of left ventricular decompression was difficult to interpret. There were no cases of heparin induced thrombocytopenia, hemolysis, or residual patent foramen ovale at decannulation. 3 patients died while on ECMO and the remainder survived to decannulation, transplant or LVAD implantation. In this case series of 15 patients on LAVA ECMO, while twelve patients survived to decannulation, transplant or LVAD implantation, only 4 were still alive at six months.

Conclusions: This is the first case series to present a majority of patients who underwent LAVA ECMO as their initial cannulation strategy. There were no cases of heparin induced thrombocytopenia, or hemolysis or residual patent foramen ovale after decannulation. While 80% of patients survived to decannulation, only 27% survived 6 months underscoring the prolonged period of high risk of mortality associated in these patients.

Keywords: ECMO, cardiogenic shock, myocardial recovery.

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I. Introduction

Veno-arterial extracorporteal membrane oxygenation (VA ECMO) is a method of temporary mechanical circulatory support that is increasingly being used in the setting of cardiogenic shock[1]. The role of the ECMO circuit is to circulate blood in order to provide end organ perfusion all while decreasing myocardial work load[2]. The ultimate goal is to achieve either myocardial recovery and weaning form circulatory support or, if that is not possible, transition to transplant or durable mechanical circulatory support (such as with an intracorporeal left ventricular assist device). In order to allow myocardial recovery, myocardial work load must be decreased and that occurs by maintaining the left ventricle decompressed[3]. When centrally cannulated placement of a left ventricular vent is not so arduous (typically via the right superior pulmonary vein), but in a peripheral cannulation strategy it is more complicated to "unload" the left ventricle. While unloading the left ventricle might be complicated, it is necessary. A growing body of literature suggests that early left ventricular venting may improve outcomes on ECMO. [4–6] There are several ways to achieve left ventricular decompression while on peripheral VA ECMO. These include the placement of an extra cardiac devices such as an intra-aortic balloon pump[5], as well as the placement of intracardiac devices such as an impella[7]. Vents can also be placed either directly across the aortic valve with a trans aortic valve pigtail percutaneously[8] or through a minimally invasive transthoracic approach such as video-assisted thoracoscopic surgical placement of a pigtail in the pulmonary vein[9] leading into the left atrium or a direct approach to the LV apex[10]. Even an interatrial septostomy can be performed to allow for decompression of the left side of the heart[11]. Finally, the venous drainage cannula to the ECMO circuit can serve as an LV vent as well if it is placed across the interatrial septum to act as a drainage

cannula of both the left atrium and the right atrium[12]. Currently no studies exist to show benefit of one venting strategy over another.

The purpose of this study is to describe a single institution case series of fifteen consecutive patients who were placed on LAVA ECMO. We describe both echocardiographic outcomes such as change in ventricular size, as well as clinical outcomes such as discharge disposition and ultimate cardiac outcome. The primary outcome of interest is six month survival. As a non-comparison study this study will not provide information regarding the superiority of this venting strategy over other strategies, but rather will be an important addition to the physiologic changes and potential clinical outcomes of using LAVA ECMO.

II. Methods

a) Description of the procedure

An 8Fr sheath is placed in the common femoral vein using ultrasound guidance. Heparin is given for a goal activated clotting time of approximately 250 seconds. A Baylis trans-septal sheath is placed in to the right atrium. A Baylis needle is inserted through a LAMP sheath and then used to puncture the interatrial septum about 1cm superior to the fossa ovalis and the sheath is advanced over the needle. The location of the puncture is identified using fluoroscopy and trans-esophageal echocardiography. Left atrial pressures are measured. The Baylis sheath is exchanged over an Amplatz guide wire and the ECMO cannula is placed. The cannula itself is a multistage cannula the possible sizes include 21-25Fr with a length of 65cm.

b) Patient Population

This is a case series of all patients who underwent ventricular decompression with placement of a trans-atrial septal venous drainage cannula while on peripheral VA ECMO between January 2018 and June 2022. All consecutive patients were included. Patients were included both if they were initially cannulated using the LAVA ECMO technique and if they were cannulated peripherally with no left atrial cannula and subsequently were converted to LAVA ECMO. The Institutional Review Board of our institution reviewed this study and granted an exemption from informed consent due to the de-identified nature of the research. The IRB number is 21-0054.

c) Statistical Analysis

The primary outcome measure was six month survival. Additional outcome measures included echocardiographic data such as degree of mitral regurgitation, right ventricular dysfunction, and left ventricular end diastolic diameter, hemolysis laboratory data, and clinical outcomes such as length of stay, and ultimate cardiac outcome (transplantation, decannulation, etc.). In addition, cost information is provided regarding LAVA ECMO. Left ventricular end diastolic diameter was measured by transthoracic echocardiogram (TTE) pre ECMO and by transeopshageal echocardiogram (TEE) post ECMO. The posterior to anterior dimension was used in TEE to measure LVEDD to more accurately correlate to TTE LVEDD. Descriptive statistical analysis was performed using Excel.

III. Results

Fifteen patients were cannulated for VA ECMO at our institution between January 2018 and June 2022. Baseline demographics of the study population are detailed in Table 1. The majority of patients were cannulated with an initial cannulation strategy of LAVA ECMO. Three patients were converted to LAVA ECMO after initial ECMO cannulation. Two patients were transferred from another institution and were converted to LAVA ECMO in the days following transfer. One patient was peripherally cannulated at the time of cardiac arrest and was subsequently converted to LAVA ECMO. The majority of patients had few significant comorbidities such as vascular disease, chronic obstructive pulmonary disease, and diabetes. Two patients presented with frozen mechanical bioprosthetic valves in the setting of not taking coumadin. Four patients (27%) were alive six months post decannulation.

The echocardiographic data obtained from the study patients pre and post cannulation for LAVA ECMO is listed in Table 2. A total of six patients (40%) were missing data that resulted in the inability to calculate a change in left ventricular end diastolic diameter. Of the patients who had echocardiographic assessment of LVEDD (8 total), the majority of patients did not have a change in LVEDD that was greater than 1.0cm (N=6, 75%). Only two patients had a decrease in ventricular diameter that was greater than 1.0cm (25%). The degree of mitral regurgitation significantly improved in 9 out of 12 patients (75%) and stayed the same in the remaining three patients. Regarding laboratory data, there were no cases of heparin induced thrombocytopenia or of hemolysis leading to circuit change. Trends in total bilirubin and platelet count are graphically represented in Figures 1 and 2. The median change in platelets went from 140,000 to 70,000 by the fifth day of ECMO. The median change in total bilirubin was 1.3 to 2.4 mg/dL. On average patients received 1.7 units of packed red blood cells in the first five days on ECMO. Half of the patients (N=8, 53%)) did not require any blood transfusion the first five days on ECMO.

Clinical outcomes of the case series are detailed in Table 3. The most common complication was vascular complications (deep vein thrombosis or limb ischemia). Three patients (20%) died on ECMO and the remainder survived to decannulation, left ventricular

assist device placement, or heart transplant. A total of six patients (three additional patients) died prior to discharge. For those who did not undergo transplant or LVAD there was no residual patent foramen ovale seen on subsequent echocardiographic assessment. For patients who underwent LVAD placement, the patent foramen ovale was closed at the time of LVAD implant.

The cost of LAVA ECMO initiation at our institution is $4,446 which is the cost of the supplies used to perform the atrial septostomy in the catheterization laboratory. This does not include the cost of the ECMO pump or ECMO personnel or cost of the catheterization laboratory operation costs.

IV. Discussion

This single institution case series of fifteen patients who were on LAVA ECMO presents valuable clinical information to the mechanical circulatory support community. First, it consists of a case series of a patients who presented in cardiogenic shock of several etiologies and suggests that this cannulation strategy can be used as the go-to cannulation strategy for peripheral VA-ECMO. Indeed, it was the initial cannulation strategy for 12 out of the 15 patients. Second, it provides the first trend in data on platelet count and bilirubin in patients on LAVA ECMO. Importantly, these trends show downward trend in platelets and upward trend in bilirubin, but these changes are not dramatic and do not compromise end organ function or circuit integrity. This would be interesting to compare to patients with an Impella device as their venting strategy. Third, it provides short and medium term clinical outcomes of LAVA ECMO patients in granular detail not previously published. While the majority of patients survived the course on ECMO, only 60% survived until discharge and only 27% were alive at six months. The continued high mortality after decannulation points to an important opportunity for outcomes improvement.

Other authors have reported case series in LAVA ECMO. The largest case series to date by far is by the Kim et al group from the University of Ulsan in Korea[13], who compared their outcomes in 62 patients who underwent LAVA ECMO with 62 patients at their institution who were on ECMO with no venting strategy. They describe 60% of their patients were weaned from ECMO and 30% survived to heart transplantation. These patients were cannulated peripherally initially and percutaneous drainage was initiated if pulmonary edema was noted on chest x-ray. While our study is not a comparison study like theirs between LV venting and no LV venting, we do report similar short-term results. Our results also provide additional data on patients who were cannulated with LAVA ECMO as the *initial* cannulations strategy as well as information regarding hemolysis (which is important when comparing to other venting strategies such as Impella) and medium-term outcomes (six month survival). This adds to a recently published case series from the University of Kentucky describing 33 patients who were placed on LAVA ECMO[14], the majority of which were cannulated using LAVA ECMO as their initial cannulation strategy.

Other smaller case series exist: Alkhouli et al describe a case series of four patients[15] in whom atrial decompression was needed after initial ECMO cannulation; Na et al describe a case series of all ECMO patients, of which 15 patients were placed on LAVA ECMO after initially being cannulated for VA-ECMO; Dulnuan et al describe a case series of four patients who were placed on peripheral VA ECMO and had signs of pulmonary congestion who then underwent transseptal cannula placement that was “Y’d” into the drainage system, but who continued to have persistent pulmonary edema. They exchanged the smaller transseptal cannula for a single venous drainage cannula. They are the first group, to our knowledge, to use the term LAVA ECMO. In summary, while many case reports exist describing transseptal puncture for LAVA ECMO in the setting of pulmonary edema once already being cannulated for peripheral VA ECMO, our study is the first to describe a case series with the majority of patients who were placed on LAVA ECMO as the initial cannulation strategy and to include laboratory data regarding hemolysis.

Another common venting strategy is the use of Impella (a percutaneous device that traverses the aortic valve) and provides left ventricular decompression. Some meta-analyses exist attempting to compare venting strategies such as Impella (when combined with ECMO this is often called ECPELLA)[16] and have found that ECPELLA is associated with reduced mortality when compared to non LV venting.[16] However direct comparison between LV venting strategies is not possible without a controlled randomized trial which is not likely to occur. Animal models may provide some answers, at least regarding hemodynamic data and interesting work is being done by Meani et al[17] and Stephens et al [18] to show both the benefit of venting as well as which strategy “unloads” the ventricle optimally. One concern our group, and many others have, with ECPELLA is that the device may be associated with increased risk of hemolysis. A study by Nakmura et al shows that up to 48% of patients cannulated with an ECPELLA strategy develop signs of hemolysis. The Impella type was not included in Nakmura’s analysis, and the newest Impella iterations (Impella CP) purportedly cause less cell lysis. It would be interesting to see a direct comparison in hemolysis labs between a cohort of patients cannulated with ECPELLA and with LAVA ECMO.

An additional point of comparison between ECPELLA and LAVA ECMO is cost. Both require use of the catheterization laboratory for placement and both

require use of ECMO pumps and ECMO personnel. The biggest difference in cost exists between the instruments used for the transseptal puncture for LAVA ECMO and the Impella device. This cost difference is significant. At our institution the instruments for LAVA ECMO cost $4,446 and the cost of an Impella device is $28,830. This cost combined with increased risk of hemolysis may provide further evidence that LAVA ECMO can be the primary LV venting strategy in select patients.

While we attempt to answer the question of whether or not venting is beneficial, we will have to decide what outcome measure is the best to reflect adequate venting and whether that outcome measure has an impact on clinical outcome. One parameter we chose to evaluate was left ventricular end diastolic diameter because it can be calculated both on transthoracic echocardiography and transesophageal echocardiography. In this study the majority of the post-cannula placement echocardiograms were done transesophageally and this value was compared to a value obtained on a transthoracic echocardiogram. We did use the inferior to anterior dimensions, which is most consistent with transthoracic quantification to attempt to mitigate this difference. Nonetheless, using only two dimensions limits a truly accurate assessment of left ventricular size. Perhaps a better measurement would be LV-end diastolic and systolic *area* rather than diameter, however this is obtained on three dimensional views which are not routinely obtained on routine echocardiography. Furthermore, venting is not the only parameter contributing to LV dimension – other factors are at play such as afterload, valvular dysfunction, and volume status. Indeed, LVEDD may not the best assessment of LV venting, but it is a commonly measured value pre and post cannulation and can provide an additional data point, albeit imperfect, to help assess impact of cannulation strategy on LV size.

In our study only two patients had a greater than 1.0cm decrease in their LVEDD. Importantly no patients had an increase of greater than 0.8cm. Does this suggest that only two patients needed venting? We think likely not. Unfortunately, we had significant missing variables for the primary outcome measure which limits its interpretation. Furthermore, most commonly the first echocardiographic assessment of the patient on ECMO was performed at the time of decannulation, LVAD, or transplantation, that is to say at a point that the heart has either recovered or been stabilized with LAVA ECMO. We have missed a more dramatic change in LVEDD that would have been better evaluated with bedside TTE on the first or second day after cannulation.

The limitations of this study are those of a retrospective single-institution case series. The sample size is limited which may impact both internal and external validity. A small sample size does make generalizability of results difficult. As discussed, LVEDD is a problematic surrogate of LV size and myocardial rest, although better surrogates are difficult to measure. Furthermore, we had several missing variables with echocardiographic data limiting interpretation of results. This patient sample was not controlled and so selection bias is inherent to this study. We included all patients who underwent LAVA ECMO, but other patients (post-cardiotomy, central cannulation, transfers) were on ECMO and LAVA ECMO was not used. Despite these limitations, this is the first case series of patients who underwent LAVA ECMO, with the majority having LAVA ECMO as their first cannulation strategy and this study provides new echocardiographic and laboratory data not previously published.

In summary we present a case series of fifteen patients cannulated for peripheral VA ECMO using a left atrial venous drainage cannula (LAVA ECMO). There were no instances of hemolysis or heparin induced thrombocytopenia and no requirements for circuit change. Ultimately twelve patients were decannulated, transplanted or underwent LVAD implantation from LAVA ECMO, but only four patients were still alive six months after decannulation. The low six-month survival warrants further investigation and underlines an important opportunity for clinicians to improve outcomes.

Conflicts of interest: none declared

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References Références Referencias

1. Geller BJ, Sinha SS, Kapur NK, et al. Escalating and De-escalating Temporary Mechanical Circulatory Support in Cardiogenic Shock: A Scientific Statement from the American Heart Association. Circulation. 2022; 146(6): e50-e68. doi:10.1161/CIR.0000000000001076
2. Cevasco M, Takayama H, Ando M, Garan AR, Naka Y, Takeda K. Left ventricular distension and venting strategies for patients on venoarterial extracorporeal membrane oxygenation. J Thorac Dis. 2019; 11(4): 1676-1683. doi: 10.21037/jtd.2019.03.29
3. Kapur Navin K., Davila Carlos D., Chweich Haval. Protecting the Vulnerable Left Ventricle. Circulation: Heart Failure. 2019; 12(11): e006581. doi: 10.1161/CIRCHEARTFAILURE.119.006581
4. Al-Fares Abdulrahman A., Randhawa Varinder K., Englesakis Marina, et al. Optimal Strategy and Timing of Left Ventricular Venting During Veno-Arterial Extracorporeal Life Support for Adults in Cardiogenic Shock. Circulation: Heart Failure. 2019; 12(11): e006486. doi: 10.1161/CIRCHEARTFAILURE.119.006486
5. Pan P, Yan P, Liu D, et al. Outcomes of VA-ECMO with and without Left Centricular (LV) Decompression Using Intra-Aortic Balloon Pumping

(IABP) versus Other LV Decompression Techniques: A Systematic Review and Meta-Analysis. Med Sci Monit. 2020; 26:e924009. doi: 10.12659/MSM.924009
6. Russo JJ, Aleksova N, Pitcher I, et al. Left Ventricular Unloading During Extracorporeal Membrane Oxygenation in Patients With Cardiogenic Shock. Journal of the American College of Cardiology. 2019; 73(6): 654-662. doi: 10.1016/j.jacc.2018.10.085
7. Desai SR, Hwang NC. Strategies for Left Ventricular Decompression during Venoarterial Extracorporeal Membrane Oxygenation - A Narrative Review. J Cardiothorac Vasc Anesth. 2020; 34(1): 208-218. doi:10.1053/j.jvca.2019.08.024
8. Barbone A, Malvindi PG, Ferrara P, Tarelli G. Left ventricle unloading by percutaneous pigtail during extracorporeal membrane oxygenation. Interact Cardiovasc Thorac Surg. 2011; 13(3): 293-295. doi:10.1510/icvts.2011.269795
9. Donker DW, Brodie D, Henriques JPS, Broomé M. Left ventricular unloading during veno-arterial ECMO: a review of percutaneous and surgical unloading interventions. Perfusion. 2019; 34(2): 98-105. doi: 10.1177/0267659118794112
10. Centofanti P, Attisani M, La Torre M, et al. Left Ventricular Unloading during Peripheral Extracorporeal Membrane Oxygenator Support: A Bridge To Life In Profound Cardiogenic Shock. J Extra Corpor Technol. 2017; 49(3): 201-205.
11. Strunina S, Ostadal P. Left ventricle unloading during veno-arterial extracorporeal membrane oxygenation. Current Research: Cardiology. 2016; 3(1). doi:10.4172/2368-0512.1000054
12. Dulnuan K, Guglin M, Zwischenberger J, Gurley J. LEFT ATRIAL VENO-ARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION: PERCUTANEOUS BI-ATRIAL DRAINAGE TO AVOID PULMONARY EDEMA IN PATIENTS WITH LEFT VENTRICULAR SYSTOLIC DYSFUNCTION. Journal of the American College of Cardiology. 2018; 71(11): A1358. doi: 10.1016/S0735-1097(18)31899-0
13. Kim AR, Park H, Lee SE, et al. Outcomes of left ventricular unloading with a transseptal cannula during extracorporeal membrane oxygenation in adults. Artif Organs. 2021; 45(4): 390-398. doi: 10.1111/aor.13838
14. Phillip R, Howard J, Hawamdeh H, Tribble T, Gurley J, Saha S. Left Atrial Veno-Arterial Extracorporeal Membrane Oxygenation Case Series: A Single-Center Experience. J Surg Res. 2023; 281: 238-244. doi:10.1016/j.jss.2022.08.020
15. Alkhouli M, Narins CR, Lehoux J, Knight PA, Waits B, Ling FS. Percutaneous Decompression of the Left Ventricle in Cardiogenic Shock Patients on Venoarterial Extracorporeal Membrane Oxygenation. J Card Surg. 2016; 31(3): 177-182. doi: 10.1111/jocs.12696
16. Fiorelli F, Panoulas V. Impella as unloading strategy during VA-ECMO: systematic review and meta-analysis. Reviews in Cardiovascular Medicine. 2021; 22(4): 1503-1511. doi:10.31083/j.rcm2204154
17. Meani P, Mlcek M, Kowalewski M, et al. Trans-aortic or pulmonary artery drainage for left ventricular unloading and veno-arterial extracorporeal life support: a porcine cardiogenic shock model. Semin Thorac Cardiovasc Surg. Published online November 7, 2020. doi: 10.1053/j.semtcvs.2020.11.001
18. Stephens AF, Wanigasekara D, Pellegrino VA, et al. Comparison of Circulatory Unloading Techniques for Venoarterial Extracorporeal Membrane Oxygenation. ASAIO J. 2021; 67(6): 623-631. doi: 10.1097/MAT.0000000000001268

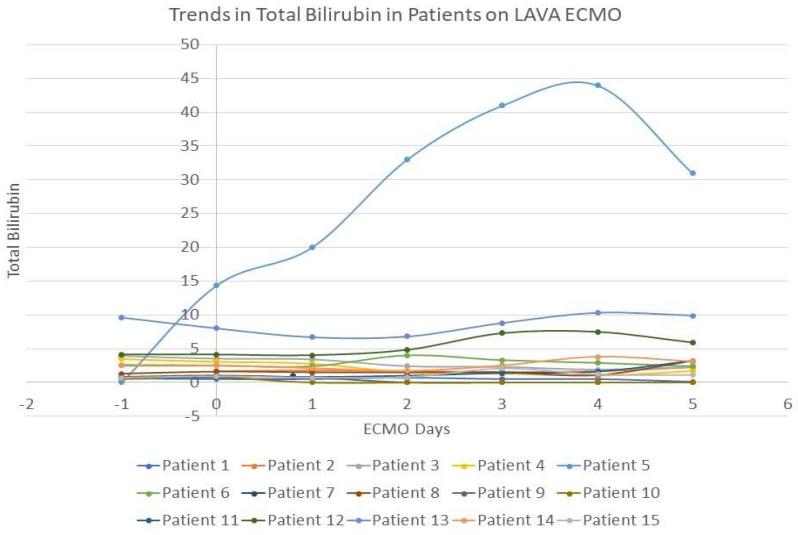


Figure 1: Trends in Total Bilirubin in Patients on LAVA ECMO

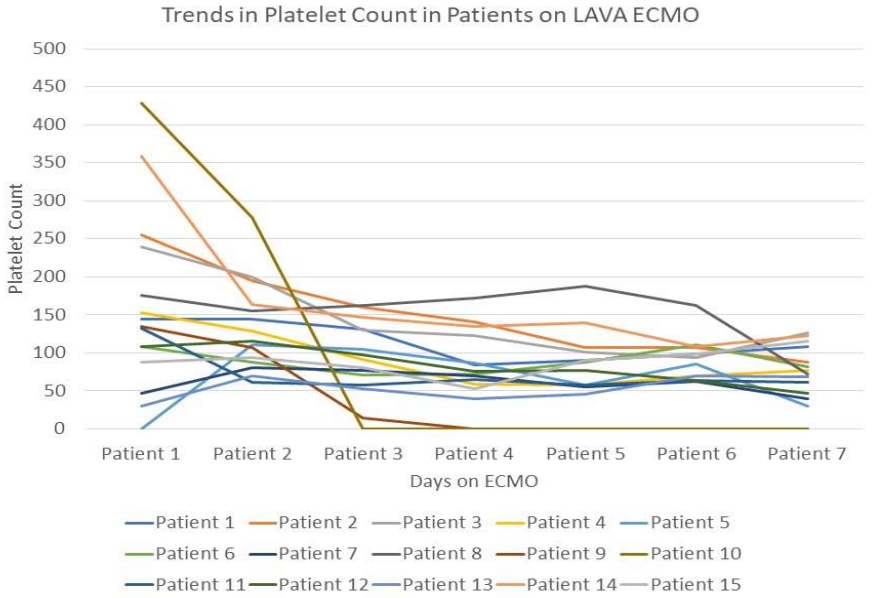


Figure 2: Trends in Platelet Count in Patients on LAVA ECMO

Table 1: Demographic Data

Table 1. Demographic data

	Median/N	IQR/%
Age (years)	49	25
Female	6	40%
Renal Disease	3	20%
COPD	1	7%
Vascular disease	1	7%
Diabetes Mellitus	5	33%
Infection	2	14%
Independent	14	93%
Ischemic cardiomyopathy	4	26%
Initial cannulation strategy	12	80%
Timing HF < 1 week	4	26%
Timing HF > 2 years	7	46%
Home inotrope	1	7%
AICD	8	53%

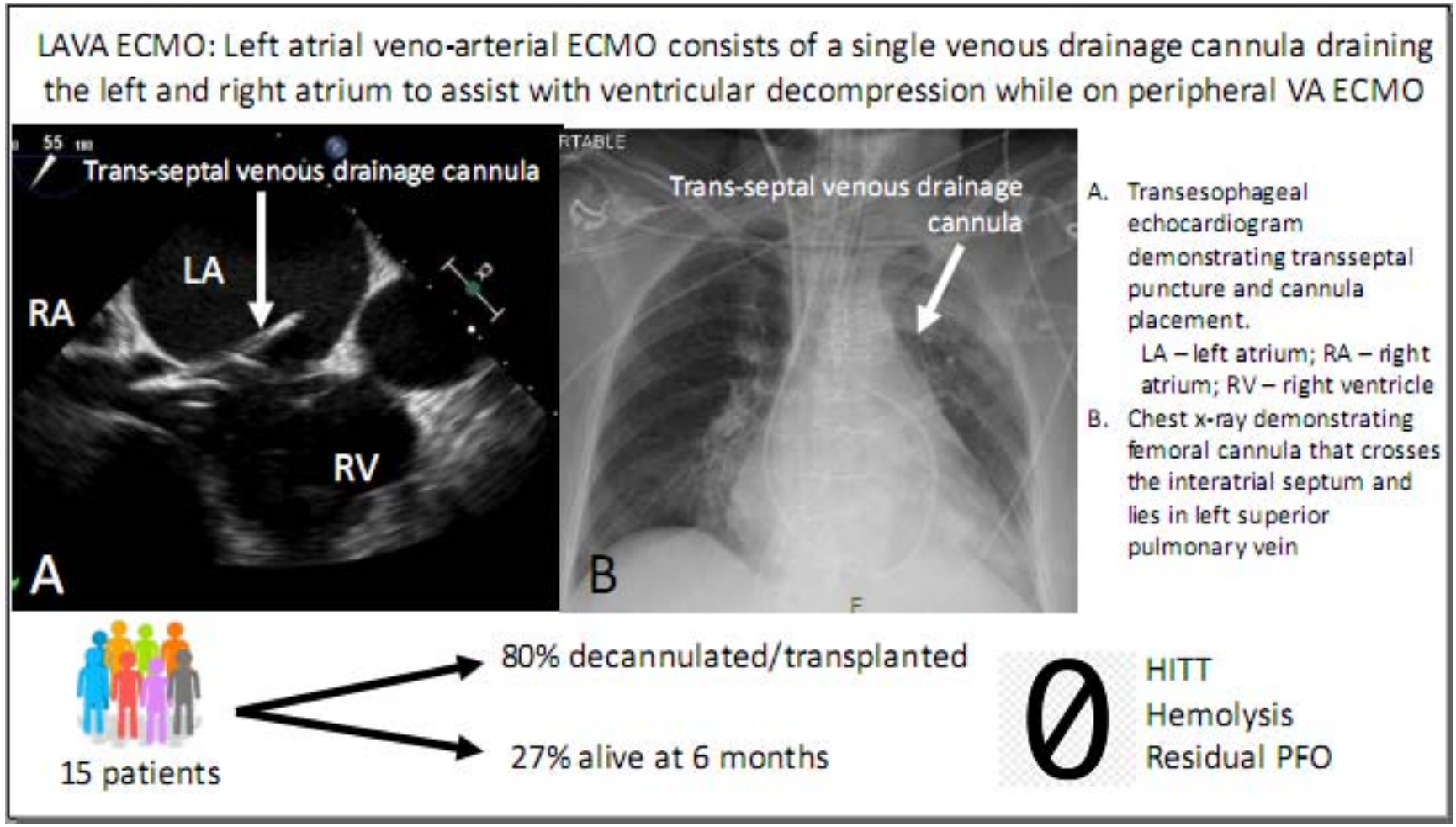
Abbreviations: AICD: automatic implantable cardioverter-defibrillator; HF: heart failure

Table 2: Echocardiographic data

Table 2. Echocardiographic Data								
	PRE				POST			
	LVEDD	LVESD	MR	RV dysfunction	LVEDD	LVESD	MR	RV dysfunction
Patient 1	4.5	3.9	mild	mild	NA	NA	none	Mild
Patient 2	5.5	5.2	none	moderate	5.9	5.6	none	severe
Patient 3	6.5	5.7	severe	none	6.9	6.5	mild	moderate
Patient 4	10.4	9.4	severe	moderate	8	7.6	trace	severe
Patient 5	NA	NA	severe	severe	NA	NA	NA	NA
Patient 6	8.5	7.9	severe	moderate	7.9	7.9	mild	moderate
Patient 7	NA	NA	NA	severe	NA	NA	NA	NA
Patient 8	6.2	4.5	severe	moderate	NA	NA	moderate	mild
Patient 9	7.4	6.7	mild	mild	NA	NA	NA	NA
Patient 10	7.3	6	mild	none	NA	NA	NA	NA
Patient 11	3.8	2.6	none	mild	4.6	3.7	none	mild
Patient 12	6.6	6.1	moderate	moderate	5.4	3.7	mild	mild
Patient 13	6.5	6.1	moderate	moderate	NA	NA	mild	severe
Patient 14	6.4	6	moderate	severe	6.9	6.5	mild	mild
Patient 15	6.7	6.1	trace	mild	6.5	6.5	trace	mild
Total	6.5	6			6.7	6.5		
Abbreviations: LVEDD: left ventricular end diastolic dimension; LVESD: left ventricular end systolic dimension; MR: mitral regurgitation; RV: right ventricle: NA not available								

Table 3: Outcomes of LAVA ECMO patients

Outcomes	n	%
Death	6	40%
Length of ECMO	9	6
Length of stay	56	38
Adverse events		
Neurologic	3	20%
Renal failure	5	33%
Respiratory failure	6	40%
Vascular complication	8	53%
Cardiac outcome		
Decannulation	5	33%
Transplantation	3	13%
LVAD	4	33%
Death on ECMO	3	20%
Discharge disposition		
Died in hospital	6	40%
Rehab	4	27%
Transfer	2	13%
Home	2	13%
ASD	0	0%
Alive at 6 months	4	27%



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Preferred Author Guidelines

We accept the manuscript submissions in any standard (generic) format.

We typeset manuscripts using advanced typesetting tools like Adobe In Design, CorelDraw, TeXnicCenter, and TeXStudio. We usually recommend authors submit their research using any standard format they are comfortable with, and let Global Journals do the rest.

Alternatively, you can download our basic template from https://globaljournals.org/Template

Authors should submit their complete paper/article, including text illustrations, graphics, conclusions, artwork, and tables. Authors who are not able to submit manuscript using the form above can email the manuscript department at submit@globaljournals.org or get in touch with chiefeditor@globaljournals.org if they wish to send the abstract before submission.

Before and during Submission

Authors must ensure the information provided during the submission of a paper is authentic. Please go through the following checklist before submitting:

1. Authors must go through the complete author guideline and understand and *agree to Global Journals' ethics and code of conduct,* along with author responsibilities.
2. Authors must accept the privacy policy, terms, and conditions of Global Journals.
3. Ensure corresponding author's email address and postal address are accurate and reachable.
4. Manuscript to be submitted must include keywords, an abstract, a paper title, co-author(s') names and details (email address, name, phone number, and institution), figures and illustrations in vector format including appropriate captions, tables, including titles and footnotes, a conclusion, results, acknowledgments and references.
5. Authors should submit paper in a ZIP archive if any supplementary files are required along with the paper.
6. Proper permissions must be acquired for the use of any copyrighted material.
7. Manuscript submitted *must not have been submitted or published elsewhere* and all authors must be aware of the submission.

Declaration of Conflicts of Interest

It is required for authors to declare all financial, institutional, and personal relationships with other individuals and organizations that could influence (bias) their research.

Policy on Plagiarism

Plagiarism is not acceptable in Global Journals submissions at all.

Plagiarized content will not be considered for publication. We reserve the right to inform authors' institutions about plagiarism detected either before or after publication. If plagiarism is identified, we will follow COPE guidelines:

Authors are solely responsible for all the plagiarism that is found. The author must not fabricate, falsify or plagiarize existing research data. The following, if copied, will be considered plagiarism:

- Words (language)
- Ideas
- Findings
- Writings
- Diagrams
- Graphs
- Illustrations
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- Printed material
- Graphic representations
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- Electronic material
- Any other original work

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2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

Changes in Authorship

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

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Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

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Preparing your Manuscript

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.

Format Structure

It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

Title

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

Tips for writing a good quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.

Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

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Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
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References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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