REVIEW ARTICLE

The whole truth of liposuction and a hole in the heart

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Fat Embolism Syndrome (FES) involving the brain may have catastrophic complications. The syndrome has an array of presentations varying from light headedness to respiratory failure, neurocognitive deficit and death. Its pathogenesis is poorly understood however moreover is associated with an undiagnosed perforated foramen ovale also known as Patent Foramen Ovale (PFO). Fat embolism following liposuction occurs in 10%-15% of patients with PFO, even when appropriate surgical strategies have been implemented. Current consensus is that PFO screening should not be done routinely except after cryptogenic stroke. There are no current guidelines for screening regarding surgery types to prevent stroke or death. The prevalence of PFO is about 25% in the general population, which increases the risk of cryptogenic stroke by 40% to 50%. Autopsy studies determined that patent PFOs with diameters between 0.2 cm to a 0.5 cm maximum dimension were present in 29% of cases, and PFO with a diameter of 0.6 cm to 1.0 cm in 6% of cases. There is no current treatment for FES or stroke other than supportive care in the setting of neurological impairment. A higher risk procedure that can be associated with fat embolism may be liposuction. Liposuction is one of the most commonly performed procedures in cosmetic and plastic surgery in the developed world. The number of procedures performed has steadily increased in the last five years representing 20% of all surgeries combined, placing it in the top three most requested procedures over the last five years. Doctors have a duty of care to ensure safest surgical outcomes. It is proposed that assessment for PFO should be considered for liposuction or other surgery that carry higher risk of FES. When considering primum non nocere, which is a double edged sword that every cure or intervention may involve potential harm, should a significant PFO be diagnosed before significant surgery, then the significant harm may be avoided.

Key Words: *fat embolism syndrome: liposuction; patent foramen ovale, lipoedema,*

INTRODUCTION

With the number of liposuction techniques increasing worldwide, one of the most concerning complications are fat embolism syndrome. Fat embolism syndrome is a disabling complication that has an array of presentations varying from mild light headedness to respiratory failure, neurocognitive deficit and death [1]. It is often associated with an undiagnosed perforated foramen ovale also known as Patent Foramen Ovale (PFO).

PFO is a potentially life-threatening condition for which patients frequently do not get medical advice or medical attention until it is too late. More than 25% of adults have a PFO. It represents the most common right-to-left shunt by encompassing 95% of the atrial septal abnormalities [2]. Fat embolism following liposuction occurs in 10%-15% of patients with PFO, even when appropriate prevention strategies have been implemented [3].

One of the most common clinical presentations of PFO is medically resistant migraine, which adversely affects the quality of life and productivity of the patient. Its impact can be measured by the level of resource utilisation, or by direct and indirect cost [4]. In some pathologies such as lipedema, patients tend to have an above-average level of subcutaneous fat where a substantial amount of fat (5 litres or more) can be removed in a single procedure. Liposuction complications are strongly correlated with the amount of fat removed during each liposuction procedure [5]. The rate of risk for these complications increases by as much as three times more per procedure. In fact, a high BMI or increased weight with PFO is a potential risk factor for not only liposuction but any surgical procedure. Current consensus is that PFO screening should not be done routinely except after cryptogenic stroke [2]. There are no current guidelines for screening regarding surgery types to prevent stroke or death.

This article will focus on the risk of fat embolism syndrome with PFO in the context of water jet assisted liposuction for lipoedema with a protocol to treat the diseased lipoedemic fat so it does not return.

LITERATURE REVIEW

Perforated/Patent Foramen Ovale [PFO] is a hole in the heart. There are two types of holes in the heart. First an Atrial Septal Defect [ASD], second a [PFO]. Although both are holes in the atrial septum, their aetiologies are different. An ASD is a congenital heart defect due to a failure of the septal tissue to form between the atria. In practice, an ASD hole is larger than of a PFO. The larger the hole, the more likely for the patient to be symptomatic [6]. During the foetal life, normal shunting of oxygenated blood occurs from the umbilical vein to the left atrium via the foramen ovale. At birth, the instant increase in pressure in the pulmonary blood flow due to spontaneous ventilation leads to an increase in the venous return to the left atrium. Following the distension of the left atrium along with a decrease of the vena caval flow into the right atrium, there is a drop in the pulmonary vascular resistance. In normal circumstances, these hemodynamic changes lead to the closure of the foramen ovale. A deficiency in the closure of the septum results in a PFO. Most people with a PFO will not have any symptoms. However, the condition may express in migraine attacks with aura or recurrent medically resistant migraine. The physiopathology by which PFO promotes migraine is obscure. One of the suggested hypotheses is that the blood which should be filtered within the lungs, is shunted from right to left, bypassing the pulmonary vascular bed and heading towards the eye and the brain. Among migraine patients, PFOs have been present up to 88% of respondents [7].

Despite thorough diagnostic evaluation, up to 45% of ischemic strokes do not have identifiable causes and are referred to as cryptogenic strokes. Numerous mechanisms have been proposed. There is an increase prevalence of PFO and ASD in these cases. As PFO is found in more than 25% of the population and studies have suggested that the annual risk of cryptogenic and recurrent strokes in patients with a PFO is 0.1% and 1% respectively, as such it is reasonable to conclude that paradoxical embolism through a PFO is the most likely stroke mechanism [2]. The embol from venous origins that enters the arterial system through the PFO, can be caused by a blood clot, air, tumour, fat or amniotic fluid.

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Patent Foramen Ovale increases the risk of arterial embolic events which includes Transient Ischemic Attack [TIA], arterial ischaemia and heart attack. This is likely feasible when a blood clot or solid particles in the venous side of the circulation move from the right side of the heart to the left through the PFO, and travel to the brain, causing a stroke, or a coronary artery causing a heart attack, as pressure increases in the chambers on the right side of the heart. In the context of TIA, this is caused by a temporary interruption of the cerebral blood flow. The symptoms are comparable to a stroke, however last less than 2 hours.

Morevover, a TIA or stroke is the first life threatening sign of a PFO. Patients younger than 55 years of age who have a cryptogenic stroke are more likely to have a PFO, also more likely to have a Deep Vein Thrombosis (DVT). In rare cases a patent foramen ovale can also cause a significant amount of blood to bypass the lungs, resulting in hypoxemia. PFO-mediated hypoxemia occurs when deoxygenated venous blood from the right atrium enters and mixes with oxygenated arterial blood in the left atrium. It is not unusual that some PFO's patients present with profound hypoxemia that is out of proportion to underlying primary lung disease, even in the presence of normal right-sided pressures. The presence of right-to-left cardiac shunting can exacerbate the degree of hypoxemia in patients with underlying pulmonary disorders.

In another context, decompression illness, which can occur in scuba diving, significant air bubbles can travel through a patent foramen ovale. The lungs are an effective filter, but a PFO is a highway for gas bubbles to bypass this filter and enter the arterial system. This paradoxical embolism is emphasised by the Valsalva manoeuvre during diving where the pressure differential between the arterial left side, the right atrium is higher than the venous right side, causing the right atrium to fill before the left atrium. Unfortunately, the peak time for bubble liberation is 30 min to 60 min post-dive, corresponding to the time when divers climb back to the boat, lifting heavy scuba related kit, and unconsciously performing Valsalva manoeuvre. These phenomena result in a syncope or a life-threatening stroke.

Acute Ischemic Stroke has also been seen in patients with renal cell Carcinoma [4]. Tumour emboli rarely cause stroke and myocardial infarction; however in the context of PFO, they have been responsible for dramatic aftermaths. Lung carcinoma has been registered as the most common source of coronary malignant tumor emboli. However, renal cell carcinoma is sadly also another common source. In this review [4] a 55-year-old woman who was diagnosed with right renal mass and cavoatrial tumor thrombus was transferred for surgical resection. An intraoperative transesophageal echocardiogram confirmed the absence of tumor thrombus from the inferior vena cava and right atrium and identified a PFO. Upon weaning sedation, she acquired left hemiplegia. The head CT scan revealed extensive hypo-attenuation in the right middle and left posterior cerebral artery territories with associated cerebral edema. In the context of this devastating neurological injury, her family elected to transition to comfort care and the patient died seven days after the surgery. This was the first reported case of intraoperative paradoxical embolism in the setting of renal cell carcinoma and PFO. It was acknowledged that the presence of PFO is a risk factor for severe cerebrovascular complications in the surgical management of renal cell carcinoma with venous involvement [4].

More tragically, an amniotic fluid embolus may travel directly from the venous to the arterial circulation via the PFO, leading to multiple cerebral infarctions. Amniotic fluid embolism is a rare syndrome; however, the complications include cardiorespiratory failure, disseminated intra-vascular coagulation, seizures, neurological deficits, and death. In this review a 34-year-old woman had amniotic fluid embolism complicated by paradoxical embolism and disseminated intravascular coagulation following an emergency caesarean section. The surgical team reacted quickly and performed cardiopulmonary bypass with with removal of the clot from the atria and closure of the patent foramen ovale. The mother and the baby survived. In another literature review, a 32-year-old woman presented to the emergency room after experiencing convulsions during labour which raised the suspicion of an acute stroke. A brain MRI revealed multiple territory embolic infarctions, the transcranial. Doppler with bubble study demonstrated a right-to-left shunt during the valsalva manoeuvre. A transesophageal echocardiogram revealed a PFO with a right-to-left shunt. The elevated intrathoracic pressure during labour may have caused blood to shunt blood from the right side to the left through the PFO. These examples illustrate how an amniotic fluid embolus may travel directly from the venous to the arterial circulation via the PFO, leading to multiple cerebral infarctions. Fat is another source of embols. Like for other causes, Cerebral Fat Embolism (CFE), occurs after fat emboli enter the arterial circulation. The presence of fat particles within the arterial system is called fat embolism, the systemic manifestation of fat emboli in the arteries is Fat Embolus Syndrome FES. Common clinical manifestations include respiratory distress, altered mental status, and rash.

FES is mostly associated with orthopaedic trauma. Bone marrow transplantation, osteomyelitis, pancreatitis, alcoholic fatty liver, and even liposuction have been procedure where FES have been reported [6]. Since most cases of FES occur following orthopaedic trauma, available research has focused on FES in orthopaedic trauma patients. Fat embolism can occur at any level of the microcirculation but tend to affect mainly the pulmonary system. FES is a multiorgan disease and can damage any microcirculatory system within the body including the brain, the skin, the eyes or the heart [7].

The clinical presentation of pulmonary fat embolism can vary greatly, ranging from slight dyspnea, tachycardia, elevated temperature, and petechiae on the skin to severe cases of respiratory distress. FES can present clinically from asymptomatic to fulminant cases which explains how it can be misdiagnosed or undiagnosed [4-8]. Fat emboli can alter their shape to pass through pulmonary precapillary shunts or directly across the pulmonary-capillary bed [9]. However, the occurrence of paradoxical embolism in some patients with FES has been correlated to the presence of PFO [10] and with an associated worse outcome. Fat emboli could lead to an increase in right ventricular filling pressures by obstructing pulmonary capillaries, thereby favouring right-to-left shunting in patients with PFO. Fat Embolism Syndrome (FES) after liposuction is potentially a life-threatening disorder, even if its incidence is low. The three chief clinical manifestations include respiratory insufficiency, cerebral involvement, and petechial rash. Although FES is a multisystemic disorder, the most seriously affected organs are the lungs, brain, cardiovascular system, and skin. Although the exact risk of developing fat pulmonary embolism is still controversial through studies or literature review, death occurs in 15% of diagnosed cases. This leads to a controversial question: how many subclinical cases have been undiagnosed so far literature reviews reveal that fat embolism detected with ETO may be observed in more than 40 percent of patients undergoing major orthopaedic procedures [11]. This raises the suspicion that the presence of a patent foramen ovale (PFO) could worsen the prognosis of FES by allowing a larger embolic load to reach the arterial circulation [12] causing severe cerebral complications, including death [13-15]. Mortality from FES can be as high as 20% [9], whilst PFO can cause a 10-fold increase in mortality and a 5-fold increased risk of major adverse advents. Another higher risk procedure that can be associated with fat embolism is liposuction [16]. Liposuction is one of the most performed procedures in cosmetic and plastic surgery. The number of procedures being performed has steadily increases in the last 5 years to represent 20% of all surgeries combined, placing it in the top 3 most requested procedures in the last 5 years [16,17]. Because of its popularity, there has also been an increase in complications following surgery. During liposuction, blood vessels are disrupted, leaving a path for the fatty acids to enter the vascular system [14,17,18]. The total complication rate of liposuction is approximately 5%, with most complications being minor [16-18] However, studies have revealed that deaths secondary to this procedure are as high as 1 in 5,000 surgeries [16-18]. Whilst liposuction is thriving in the cosmetic world, liposuction derived techniques are becoming used to treat disabling medical condition such as lipoedema.

Lipoedema is a chronic, progressive and considerably disabling condition that primarily affects women. Pain is the leading symptom of lipedema with an estimated incidence of 10% [19]. This condition is affecting millions of women who have an impaired quality of life and associated depression as a result of cosmetic and physical part of the disease [20]. The primary focus of treatment is to reduce its related lower extremity symptoms, disability, and

functional limitations of the limbs, primarily of the arms by removing the inflammatory fat to improve patients' quality of life, as well as preventing disease progression.

Management of lipoedema has been divided into conservative therapy and surgical interventions. The conservative therapy includes an adjusted diet by avoiding inflammatory foods and reduction of secondary obesity, Combined Decongestive Therapy (CDT) through manual lymphatic drainage and compression garments. Surgical intervention is preferably performed by Water Assisted Liposuction (WAL)[21]. It is the treatment of choice for patients to progress beyond conservative measures. Water assisted liposuction uses a pressure spray of tumescent fluid to dislodge the fat from the connective tissue using a fine cannula. As per any form of liposuction, a fat embolus (fine or large) could break free, travel in the blood stream and ends up being, lodged almost anywhere in the body, resulting in an interruption of the blood supply in the involved organ. Fat emboli can break down in smaller parts, which can affect several organs at the same time and lead to multiple organ failure. This complication is known as fulminant fat embolism syndrome. Most likely small emboli do not cause any clinically manifestation as they are most likely broken up as smaller particles as they migrate in the blood stream and filtered in the lungs. Only a small fraction will turn into FES. The risk of having serious complications is intrinsically linked to a widely patent PFO allowing significant right to left shunting of blood with the potential of FES and fatality.

Although PFO's are linked to a syndrome that includes debilitating migraine, brain fog and exercise intolerance [7]. Problems arise when blood contains an embolus, thrombus or fat, which can lead to Cardioembolic cerebrovascular Accidents (CVAs) and Transient Ischaemic Attacks (TIAs). PFO is the major cause of stroke in younger patients [2]. Dramatic and serious sequalae even death arises when a PFO (average diameter of 4.9 mm) allows the passage of emboli from the venous system that are large enough to occlude the initial part of the middle cerebral artery (3 mm) [19]. In the USA, 345,000 patients aged 18–60 years have been diagnosed with PFO related cryptogenic stroke [2,22]. These are brain infarctions not linked to arteriosclerosis, (small vessel disease), rather cardio-embolism [23] and constitutes up to 40% of all ischemic strokes [24].

As described earlier, the prevalence of PFO is about 25 percent in the general population, which increases the risk of cryptogenic stroke by 40 to 50 percent in patients. Autopsy studies determined that patent PFOs with diameters between 0.2 cm to a 0.5 cm maximum dimension were present in 29% of the cases, and patent PFO with a diameter of 0.6 cm to 1.0 cm was in 6% of them [25]. A second study of 965 patients recorded a PFO incidence of 27.3%, with PFOs varying in size from 1 mm to 19 mm with an average of 4.9 mm. Those studies drew an interesting conclusion that the incidence of PFO declined with age, suggesting that anatomic closure may occur even in adulthood. [24,25] Konstantinides found that patients with a PFO had a significantly higher incidence of ischemic stroke (13% versus 2.2%) and peripheral arterial embolism (15% versus 0%) than patients without a PFO [26]. The literature review of Kellogg et al. revealed that 98% of the patients presented with mental status changes had a relatively good outcome [26,27]. The overall mortality was 7.4%, and the remaining cases had good outcomes, with intact or mild disability in 72.2% out of the 54 cases [26,27]. Another study on PFO and ischemic stroke in patients with PE found that ischemic stroke was more frequent in the PFO group (21.4%) than in the non-PFO group (5.5%) [26,27]. Dermal involvement, such as petechial rash, has been reported inapproximately 50% to 60% of patients; this tends to be transient lasting 4 to 6 hours [27,28]. Retinal lesions are seen in 50% of patients and are self-limiting, oftendisappearing within weeks [27,28]. PFO is also seen in a quarter of patients with idiopathic pulmonary arterial hypertension and is associated with increased prevalence of severe hypoxemia [28].

While PFO is becoming recognised worldwide as a cause for cryptogenic cerebrovascular events, there are other situations in which documenting a right to left shunt is important. The accepted belief in the medical community is that the presence of a PFO seems to carry no clinical or survival benefit for normal individuals despite the understanding that PFO has a causative role in several medical entities such as cryptogenic stroke, migraine with aura, and decompression disease. Although in normal individuals, diving activities could warrant PFO detection. The presence of a large PFO is linked with severe unexplained decompression sickness through paradoxical gas embolism [29-32]. The incidence of a first stroke in individuals with and without PFO is similar, which is approximately 1% per year. However, the yearly risk of a recurrent stroke in patients with PFO is raising incrementally by 1% per year [31-33].

Transoesophageal Echocardiography (TOE) has been for a long time regarded as the gold standard imaging procedure for patients with suspected right-to-left shunting [34]. However, there are some limitations of TOE that Trans Cranial Doppler (TCD) imaging overcomes. One of the strengths of TCD is its ability to recreate a dynamic recording of paradoxical embolism through an agitated saline contrast medium injected into a peripheral vein during the strain phase of the Valsalva manoeuvre while the middle cerebral artery is sonographically monitored with doppler imaging during the release phase [35]. A literature review confirmed the diagnostic accuracy of TCD in PFO diagnosis versus TOE under normal breathing. The sensitivity and specificity of TCD has been found in several studies to be 96.1% and 92.4% respectively, whereas the respective measures for TOE were 45.1% and 99.6% respectively. TOE was superior in terms of higher positive likelihood ratio values whereas TCD demonstrated lower negative likelihood values compared to TOE [33]. The conclusion was that TCD appears to be more sensitive than TOE to detect a right to left shunt due to the conscious state of a patient during a TCD and to effect a forceful valsalva manouevre compared to the general anaesthetic required for a TOE and an inability to perform a valsalva. The gold standard for PFO detection would be the combination of TOE and TCD [36]. Further research is required to determine appropriate guidelines for first line testing to detect intravascular shunting [37] either by TOE or TCD [37,38], and the place of TOE in the detection and treatment of PFOs [38]. These studies will also be useful in high-risk cases where there is a PFO as well as a thrombophilia which significantly raises the risk of stroke.

When considering treatment and correction of PFOs, there are currently two approaches for closure: surgical and transcatheter closure [39,40]. Current practise for treatment is only considered after a dramatic event has occurred such as stroke related to PFO. However, patients may benefit from closure through early detection. Medical misadventure can be avoided in the context of PFO diagnosis and percutaneous closure where procedures carry a risk of stroke. Patients with a past history of cryptogenic stroke or a long-life history of recurrent medically resistant migraines with aura have a higher risk of neurological adverse events and may benefit from preoperative screening and percutaneous closure of PFO [41-44]. There is no current treatment for FES or stroke other than supportive care in the setting of neurological impairment. In this context PFO closure should be considered for prevention of paradoxical embolism especially when there is a high safety margin with the procedure when performed by an experienced structural cardiologist [42,44,45]. Several studies showed that percutaneous PFO closure significantly reduced the risk of recurrent stroke [43-45].

More than 300 million surgeries are undertaken worldwide annually [46-48]. Each of them carries a potential risk of perioperative stroke. The prevalence of PFO in the general population, that is mostly undiagnosed is around 27% [2,49]. Studies have shown an increase risk of 60% for ischaemic stroke if the patient has a PFO [49]. Additionally, patients with varicose veins as larger conduits would allow thicker fractions of fat to travel back to the heart increasing the risk of FES. Parsi noted 13 documented cases of stroke following foam sclerotherapy as an alternative to stripping veins. PFO was determined as the causative factor [41] representing the right to left shunt resulting in venous embolism and stroke. Sclerotherapy is a low-risk procedure compared to more invasive procedures such as liposuction or orthopaedic surgeries. Future research would be useful to determine the risk of PFO related stroke, the procedure and the size of a PFO. Current guidelines do not support PFO screening prior to an episode of stroke. In Australia generally in the public system PFO would not be closed unless there was a stroke. As of 1st July 2021, Medicare Benefit Schedule changes now preclude PFO closure in the private health setting unless there has been a stroke. The current landscape raises medicolegal challenges where a risk of a PFO related stroke is present yet not investigated prior to surgery [50-53]. Obviously, this needs to be balanced

with the risk of PFO closure to prevent stroke especially when the procedure is considered low risk.

It may be that closure is considered for patients with significant PFO syndrome symptoms such as migraine brain fog and exercise intolerance [7,2] which points to a large PFO [53-57]. Further one may consider the importance of closing PFOs for patients especially with high risk thrombogenic histories such as thrombophilias and slower post-surgery ambulation especially where closure can be performed with high success and low risk of complications [48,49].

CONCLUSION

In conclusion, PFOs occur in 20%–30% of the general population as a result of an intracardiac anatomic variation. Knowledge regarding the association of adverse events with the disease remains lacking however it is known to be associated with debilitating migraine and stroke. This vestige of embryologic physiology is gaining more attention as it is recognised that it harbours potential catastrophic events including death. The controversy regarding the clinical significance of PFOs in the setting of surgical treatment is attracting more attention. An interdisciplinary and personalised approach to define high risk patients is required for the management of PFO especially when the risk of fat embolism syndrome is at stake. The association of PFO and the true risk of morbidity and mortality as well as the benefit of screening surgical patients require further research.

Doctors are faced with a fiduciary responsibility towards patients to ensure a safe surgery in a possible undiagnosed Patient with PFO. The primum non nocere, which is a key component of the care provided by doctors, means given the risk of PFO; it might be better no to do a surgery than to risk more harm than good. The current consensus is screening PFO is not recommended as it could lead to overdiagnosis and unnecessary closure surgery. Zaman et al. wrote a provocative paper illustrating how making overdiagnosis a priority can result in medical nihilism that is detrimental to patients. In high-risk procedures, deferring PFO detection could imply a significant risk that is not addressed in the consenting process. Carefully evaluating the benefits and risks of PFO detection and then ultimately closure of a PFO if found can provide a more robust medicolegal position where the patient understands fully all risks associated with their elective procedures.

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