Clinical Cardiology and Cardiovascular Medicine

Volumetric Overload Shocks (VOS) in the Patho-Etiology of the Adult Respiratory Distress Syndrome (ARDS): Correcting Errors and Misconceptions

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Abstract

Introduction and objective: To report critical literature analysis that shows Volumetric Overload Shock (VOS) is the real patho-etiology of the Adult Respiratory Distress Syndrome (ARDS) demonstrating multiple errors that predisposes to VOS.

Material and methods: The literature on ARDS and physiological law of Starling are critically analyzed and multiple errors and misconceptions prevailing in fluid therapy are corrected. Recent reports on VOS in the patho-etiology of ARDS are summarized.

Results: The literature on ARDS and physiological law of starling is critically analyzed revealing multiple errors and misconceptions. Starling's law is wrong as both of its forces do not work as proposed. Errors have been corrected and the hydrodynamics of porous orifice G tube are advanced as replacement for Starling's law. The evidence confirmed VOS induced by sodium-based fluids as the real patho-etiology of ARDS.

Conclusions: The critical literature analysis on ARDS and physiological law of Starling rectified many errors and misconceptions. The hydrodynamics of the G tube in a surrounding chamber C that mimics capillary-interstitial compartment, gives a real replacement for Starling's law for the capillary-interstitial fluid transfer. The VOS proved to be the real patho-etiology of ARDS.

Introduction

The Adult Respiratory Distress Syndrome (ARDS) was first reported in 1967 [1]. It was realized later that it is part of Multiple Vital Organ Dysfunction/Failure (MVOD/F) syndrome that affects hundreds of thousands cases worldwide every year and is associated with substantial morbidity, cost and mortality [2]. In the first report [1], Volumetric Overload (VO) of 12-14L was documented in every case but later reports did not incriminate VO in its patho-etiology [2,3]. With VO unsuspected, the results of both Randomized Controlled Trials (RCT) [3] and systemic reviews [2] were inconclusive. The most recent RCT investigating fluid therapy in MVOD/F aimed at the first 7 postoperative days thus missed the initiating event of bolus fluid therapy given during resuscitation or surgery that established the condition in the first place. The RCT never mentioned VO or increase in Body Weight (BW) hence the most recent systemic review totally overlooked VO as possible insult inducing ARDS [3]. The reason for overlooking VO as cause of ARDS is the accumulation of clinical misconceptions based on erroneous Starling's law on the capillary-interstitial fluid transfer [4]. This has subtly misled physicians into infusing big bolus VO for treating true or presumed hypovolaemia causing hypotension thus inducing ARDS. The role of VOS in the patho-etiology of the Transurethral Resection of the Prostate (TURP) syndrome was reported [5-12].

Historical Background

Ever since fluid therapy has proved life-saving for millions of polytrauma victims of World War Two (WW2), the procedure was transferred into clinical practice with all its success and complications without verification. Reports from WW2 and clinical practice [13] demonstrate complications of fluid therapy that is recognized today as the MVOD/F syndrome. The slogan of that era, that remains operative today, was: "Too much of a good thing must be a good thing"!? This is untrue particularly and obviously concerning water: water is essential for life yet its excess or deficiency is equally detrimental or lethal.

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The Scientific Basis of VO

The blood volume of an adult is 5l and the Cardiovascular System (CVS) capacity is 7l [14-16]. Trying to fit 10-15l of fluid in 7l capacity container, must spell fluid over! This basic physics principle should limit physiology laws on CVS volume-pressure relationship that govern fluid therapy.

One current widely received misconception is that any infused VO of plasma albumen or substitute should stay intravascular according to Starling's law on capillary-interstitial fluid equilibrium. This issue has, long and repeatedly, been proved wrong in both physiology and clinical studies demonstrating that albumen does not work [17]. It has repeatedly called for re-consideration of Starling's law [18], yet it remains operative in clinical practice on fluid therapy!

When there is true CVS volume deficit most of the infused fluid stays intravascular topping CVS volume up to normal level, while an excess VO distributes within minutes between CVS and ISF spaces with excess fluid spelling over into the third space. Flooding of the ISF space manifest mainly as trunk oedema and the cells are affected. The cells become hypoxic manifesting with the clinical features of MVOD/F while flooded lung alveoli manifest with ARDS. Also some oedematous cells may disintegrate by hydrolysis leaking its contents into the serum identified later as the Systemic Inflammatory Response Syndrome (SIRS). Advances in ventilation have improved oxygen uptake at the lung, and advances of CVS and renal support have improved prognosis, prolonged survival and modified the clinical picture of ARDS. The extra-vascular leakage of VO fluids into the ISF space is an internal flooding that cause the pathological torso and limb oedema commonly seen on ICU affecting all cases of MOVD/F. The excess fluid is confirmed by increased body weight. Patients who die go to the mortuary with it and those who recover must lose it before discharge from the ICU and hospital. Internal flooding and oedema of vital organs is obvious on the postmortem examination [7-9].

The major concern, and worry, is that most involved physicians do not consider such gross torso oedema pathological! It is even thought advantageous on the erroneous belief that over-hydration provides better oxigenation of tissues and cells! Such view overlooks the obvious difference between irrigation and flooding that makes the difference between life and death. A patient on ICU with an excess of 7-14 Kg of body fluids causing ISF and cell oedema cannot be considered as normal. The most harmful effect of VO flooding ISF space, however, is not the detectable subcutaneous oedema but is the hidden oedema affecting the vital organs manifesting clinically with MVOD/F syndrome. The clinical severity of ARDS and MVOD/F depends not only on VO quantity but also inversely on the time (t) of gain. The fluid type and tonicity are important.

Errors and misconception on fluid therapy

The errors and misconception are identified here.

Error I: Every arterial hypotension is considered synonymous with hypovolaemia or at least treated as such with volume expansion!

Correction 1: Hypotension is not synonymous with hypovolaemia. The difference between the therapeutic/ physiological VO in contrast with the paradoxes of pathological VO on arterial pressure and renal response must be precisely identified. Two paradoxical responses of pathological VO require recognition: one is inducing hypotension shock and the second is causing acute renal failure (ARF). The transition from the hypovolaemic hypotension shock into the VO hypotension shock during overzealous volume expansion occurs seamlessly unnoticed and undetected by any monitoring until it manifests later on ICU with torso oedema and increased BW of ARDS [7-12].

Error II: The volume-pressure relationship of the vascular system is perceived as infinite strait line!?

Correction II: The volume-pressure relationship particularly that of vascular volume and arterial pressure is a limited line segment, beyond which the relation collapses. Within limits, increasing vascular volume (physiological or therapeutic VO) increases arterial pressure and induce dieresis but when such limit is exceeded (pathological VO) a paradoxical hypotension and annuria occur [5, 7-12].

Error III: The right atrium or Central Venous Pressure (CVP) and Pulmonary Capillary Wedge Pressure (PCWP) as monitoring parameters guiding fluid therapy are given a value of 18 to 22 mmhg as currently practiced on many ICUs [3,13]. Although current recommendations [2,3] indicate that CVP and PCWP are unreliable and no longer being used, evidence from prevalence of ARDS on ICU testify differently, and it remain part of ARDS definition [2].

Correction III: The given figures of CVP and PCWP are erroneously too high yet remain widely practiced. Persistence to achieve such high CVP using massive volume expansion is among the misleading reasons for inducing pathological VO causing ARDS. The infused fluid rapidly shifts out of the vascular system and CVP may drop back to below 10 cm water, then another bolus VO is given before the gross torso oedema and increase BW becomes obvious. The correct CVP figures are given in all physiology textbooks that swing around 0 (at mid-axillary line) with a range of +7 to -7 cm water [14-16].

Error IV: The capillary forces responsible for irrigating and oxygenating the ISF space and cells are mixed up with that causing oedema, flooding and drowning.

Correction IV: It is strongly recommended that every physician involved in fluid therapy, ARDS management should reconsider what is the physiological function of the arterial and venous pressures. Starling reported his hypothesis at the Lancet in 1886 [4]. Being false, this hypothesis underlies most mentioned erroneous concepts on fluid therapy. Starling's hypothesis was wrongly made into physiological law later [19].

Error V: The major misconception, and unfortunately the most prevailing, is wrongly assuming that the vascular system is an all positive pressure system, in which not only the mentioned arterial volume-pressure relationship is misconceived as infinite strait line but also keeping high venous pressure and ISF tissue over-hydrated are erroneously believed to enhance cell nourishment and oxygen delivery. This is precisely the error underlying the pathological VO inducing ARDS.

Correction V: To assume that CVS to be an all positive pressure system is quite simply wrong. In fact, there is a lot of negative physiological pressure under the skin. It is well known that the pleural spaces have negative pressure and the pressure in alveoli alternates. The CVP of normal subjects may swing around Zero, between positive +7 and negative -7 mmhg [14-16]. The intracranial pressure is also negative. Thus the ISF space of subcutaneous tissues, most organs and parts of the body have negative pressure of -7 cm water that has been demonstrated [20] and re-affirmed [21] but neither considered nor satisfactorily explained.

What is Volumetric Overload (VO)?

A therapeutic volume replacement of measured blood or fluid loss causing hypotension episode or shock must be precisely calculated and replaced avoiding over-estimation. A physiological VO added to the actual measured blood loss is perhaps the safest fluid regimen during major surgery. The safest maximum acute volume expansion should

not exceed the capacitance of the vascular system of 7l by more than 1% BW. If acute volume expansion increases BW by more than 5% the risk of such pathological VO inducing ARDS is real. The type and tonicity of fluid used as well as its quantity and time of VO gain count [7-9].

A pathological VO2 of 3.5l induces moderate MVOD/F and certainly 7l is serious. For pure VO1 a bolus of 3.5-5l in <1/hour induces shock [7-12]. When the figures are transferred into percentage of BW, the plasma volume equals ≈ 3-3.5l (5% BW) of 70 kg adult. A pathological VO of ≈ 3%, 5% and 10% BW causes mild, moderate and severe ARDS, respectively. The percentage figures apply to children and women also. A pathological VO1 acutely loading the vascular system with >5%BW causes serious morbidity, or even sudden death, and is characterized by the acute dilution hyponatraemia [22,23]. It induces paradoxical hypotension shock and ARF [7-9]. A quantity of VO2 fluids ≈ 5%BW may cause subtle pathological changes but VO2 of ≈ 7-14l (10-20%BW) is that observed in cases of ARDS [1].

Volumetric Overload Shocks (VOS)

Volumetric Overload Shock (VOS) is a condition caused by massive fluid infusions in a short time [7-9] and is of two types; Type one (VOS1) and Type two (VOS2). VOS1 is induced by sodium-free fluid gain of 3.5-5 litres in one hour such as Glycine, Glucose, Mannitol and Sorbitol. It is known as the TURP syndrome [5] or hyponatraemic shock [22] that was experimentally induced in dogs [23]. VOS2 is induced by massive infusion of sodium-based fluids such as normal saline, Ringer, Hartmann, plasma, plasma substitutes and blood transfusions that may complicate the therapy of VOS1. VOS2 also complicates fluid therapy in critically ill patients suffering from other known shocks such as hypovolaemic, hemorrhagic and septicemia shocks and present with ARDS. VOS2 is induced by the gain of 12-14 litres of sodium-based fluids when reported in ARDS [1].

Two clinical studies aiming to understand the TURP syndrome and recognizing VOS were done. A prospective clinical study on 100 consecutive TURP patients of whom the condition of TURP syndrome affected 10 patients with severe hypotension and bradycardia and severe acute dilution HN of <120 mmol/l [5]. VO was the only significant factor in causing the condition. The second clinical study involved a case series of 23 cases of the TURP syndrome manifesting as VOS1 [7-9]. VO quantity and type is shown in (**Figure 1**). The first 3 cases died as they were diagnosed and treated erroneously as one of the recognized shocks and treated with further volume expansion. The remaining 20 patients were correctly diagnosed as VOS1 and treated with Hypertonic Sodium Therapy (HST) of 5% Sodium Chloride or 8.4% Sodium Bicarbonate. Each patient passed 4-5 litres of urine followed by recovery from shock and coma. This treatment was successful in curing all patients bringing them back from dead.

The physical investigation involved studies of the hydrodynamics of the porous orifice (G) tube comparing it to that of Poiseuille's tube [6,10,11]. Thousands of experimental measurements of pressures at various parts of a circulatory system incorporating the G tube in a chamber to mimic the capillary-interstitial fluid compartment. The effect of changing the proximal (arterial), the distal (venous) pressures and the diameter of the inlet on side pressure of the G tube and chamber pressure as well as the dynamic magnetic field like fluid circulation around the G tube were documented. This dynamic magnetic field like fluid circulation around the G tube and surrounding it in C chamber provides adequate replacement for Starling's law. The physiological equivalent of this physical study was done on the hind limbs of sheep [10]. It demonstrated that arterial pressure causes suction not filtration due to the effect of pre-capillary sphincter. It is the only possible explanation why the interstitial tissue pressure is negative of -7 cm water [19]. Venous pressure augmented filtration causing oedema or dropsy formation.
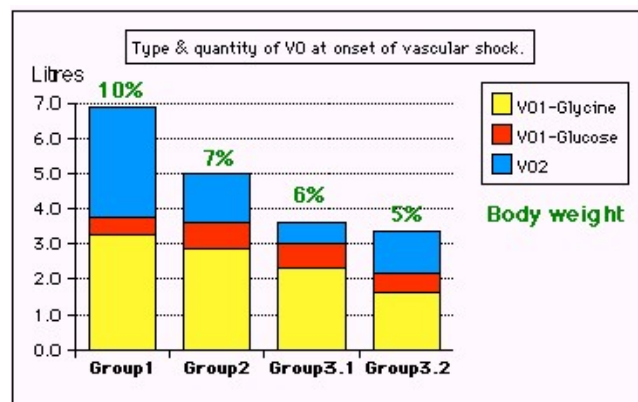

Figure 1: shows Volumetric Overload (VO) quantity (in liters and as percent of body weight) and types of fluids. Group 1 was the 3 patients who died in the case series as they were misdiagnosed as one of the previously known shocks and treated with further volume expansion. Group 2 were 10 patients from the series who were correctly diagnosed as VO shock and treated with Hypertonic Sodium Therapy (HST). Group 3 were 10 patients who were seen in the prospective study and subdivided into 2 groups; Group 3.1 of 5 patients treated with HST and Group 3.2 of 5 patients who were treated with guarded volume expansion using isotonic saline.

Shock is a disturbance at the capillary cellular level impairing the capillary-interstitial fluid transfer; hindering delivery of oxygen and removal of waste products. The process is also governed by Starling's law [4]. In this law the arterial pressure is considered the force causing capillary filtration! If this is true, how come that arterial hypertension though very common never causes oedema? Starling based his hypothesis on Poiseuille work on strait uniform brass tubes [14]. Latter evidence however demonstrated that the capillary is a porous narrow orifice (G) tube as it has a pre-capillary sphincter [24] and pores that allow the passage of plasma proteins [25]. As the capillary pores allow the passage of plasma molecules, nullifying the osmotic pressure of plasma proteins i.e. oncotic pressure does not exist in vivo, a call for reconsideration of Starling's law was previously made [18] but there was no alternative at that time.

The hydrodynamics of the G tube [6,11,12] **figure 2** demonstrated that the proximal (arterial) pressure induces a negative side pressure gradient on the wall of the G tube causing suction most prominent over the proximal half and turns into positive pressure over the distal half. Incorporating the G tube in a chamber (C), representing the interstitial space surrounding a capillary, demonstrated a rapid dynamic magnetic field-like fluid circulation between the C and G tube lumen. This is a mixing engine between C and G effecting rapid irrigation under negative pressure i.e. without flooding, oedema or dropsy formation. Incorporating the G tube and C in a circulatory model driven by electric pump inducing proximal pressure similar to arterial pressure; causing suction from C into the lumen of G tube. This proves that the arterial pressure causes suction not filtration at the capillary interstitial fluid circulation, and hence Starling's law is wrong. The reported hydrodynamics of the G tube provides an adequate mechanism for replacing Starling's law as the capillary interstitial fluid circulation [6,10,11].
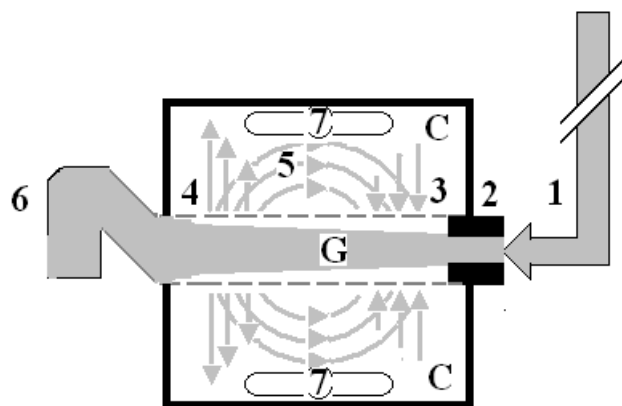
Figure 2: shows diagram of the porous orifice (G) tube enclosed in chamber (C) based on several photographs demonstrating the magnetic field-like G-C circulation phenomenon. The proximal inflow (arterial) pressure (1) pushes fluid through the orifice (2) creating fluid jet in the lumen of the G tube. The fluid jet creates negative side pressure gradient causing suction maximal over the proximal half of the G tube near the inlet (3) that sucks fluid into lumen. The side pressure gradient turns positive pushing fluid out of lumen over the distal half maximally near the outlet (4). Thus the fluid around G tube inside C moves in magnetic field-like fluid circulation (5) taking an opposite direction to lumen flow of G. tube. The inflow (arterial) pressure (1) and orifice (2) induce the negative side pressure energy creating the dynamic G-C circulation phenomenon that is rapid, autonomous and efficient in moving fluid out from the G tube lumen at (4), irrigating C at (5), then sucking it back again at (3), maintaining net negative energy pressure (7) inside C. The distal outflow (venous) pressure (6) enhances outflow at (4) and its elevation may turn the negative energy pressure (7) inside C into positive, increasing volume and pressure inside C chamber.

Why is Starling's law wrong?

The oncotic pressure of plasma proteins is the presumed absorption force responsible for returning fluid back into the capillary lumen [4,19]. Again this was based on physics experiment in which albumen was separated from water by a membrane impermeable to albumen molecules. That experiment [19], in 1948, showed an oncotic force of albumen. However, it was shown later that such oncotic force is too weak and too slow to be clinically solely responsible for fluid return from the Interstitial Fluid (ISF) space into the capillary lumen [26]. Also in 1967, it was discovered that the capillary wall is a porous membrane allowing easy free passage of plasma protein molecules in and out between the capillary lumen and ISF space. These pores identified as the inter-cellular slits [25]. The pressure in the ISF space was measured inside subcutaneously implanted chamber and proved negative of -7 cm water [20]. A similar study demonstrated that plasma protein molecules move freely between the implanted chamber and blood stream [21].

This means that clinically none of Starling forces work, certainly not in vivo! The oncotic force does not exist across porous leaky capillary membrane! [25] Albumen has long been known not to work and that called for reconsideration of Starling hypothesis [18]. More recently the BMJ made a slogan out on it "Why albumen may not work?". This was based on Cochrane Injuries Group systemic review of RCT on ARDS demonstrating that albumen does not work [17]. In Starling's law, the arterial pressure is presumed the main force responsible for filtration [14-16]. Although arterial hypertension is very common there is not a single case report in which arterial hypertension causes oedema!

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