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Complication of Fluid Therapy Causing the Acute Respiratory Distress Syndrome: Facts and Comments. The Role of Volumetric Overload Shocks in Pathoetiology

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Abstract

Objective: *To report multiple facts and comments on the acute respiratory distress syndrome (ARDS) as well as errors and misconceptions and the role of volumetric overload shocks (VOS) in its patho-etiology.*

Material and methods: *Two reports in the Lancets that represent the received views on ARDS are critically analyzed to demonstrate the overlooked facts and errors and misconceptions. Data from my own research demonstrates the role of VOS in the patho-etiology of ARDS.*

Results: *Multiple overlooked facts on ARDS and appropriate comments on it as well as errors and misconceptions on fluid therapy are reported. The role of VOS in the patho-etiology of ARDS is summarized. Underlying the reported missing facts and errors are the erroneous Starling law on the capillary-interstitial fluid transfer. The correct replacement for Starling's law is the hydrodynamic phenomenon of the porous orifice (G) tube.*

Conclusions: *ARDS is an iatrogenic complication of fluid therapy. Many overlooked facts and multiple errors and misconceptions underlie the current understanding of ARDS, Underlying all of it is the wrong physiological law of Starling on capillary interstitial fluid transfer. The correct replacement of Starling's law is the hydrodynamic phenomenon of the porous orifice (G) tube. The real patho-etiology of ARDS is VOS.*

Keywords: *Hyponatraemia, Shock, ARDS, TURP syndrome, The multiple vital organ dysfunction syndrome, Fluid therapy*

Two articles reported at The Lancet triggered the following comments. The first article is a comment updating perioperative fluid management [1] that faithfully reflected currently received views. However, it failed to identify an optimum regimen or define what is volumetric overload (VO)? The second article is a review [2] on acute lung injury and the adult respiratory distress syndrome (ARDS) recognizing it as the multiple vital organ dysfunction/ failure (MVOD/F) syndrome. It stated: "it affects hundreds of thousands of cases worldwide every year and is associated with substantial morbidity, cost and mortality". The importance of this syndrome with such staggering prevalence of morbidity and mortality was realized 25 years ago. Its dilemma might have been resolved if comments sent to The Lancet 20 years ago were taken seriously not rejected. The early warning might have attracted a fraction of the attention given to AIDS, as certainly ARDS or MVOD/F are of no lesser magnitude or importance. Hopefully as I try again now with clear evidence and facts it would be better received and reported. The pointed out errors and misconceptions are self-evident while corrections are comments based on my experience, clinical observations, research work and plausible overlooked documented evidence that remains as good as new today [3,4].

When the current rules on fluid therapy fail to provide adequate reliable guidance to practicing

physicians, perhaps a reliance on simple proven facts of physiological data, easily verifiable clinical observations and rejecting erroneous hypotheses may make better solid ground of evidence-based medicine for resolving such complex clinical dilemmas. I believe when such erroneous concepts prevail it blind researchers, thus even the best executed prospective randomized controlled trials (RCT) and systematic reviews will fail to give satisfactory answers or solutions. Its results will at best appear contradictory and confusing, though it may provide incremental advances to such enormous clinical dilemma. I believe it is time to realize that erroneous confounded understanding and misconceptions are impossible to rectify without nihilistic approach.

Fact 1

Fluid therapy is used in hospitals mainly for treating hypotension shock of serious origin such as haemorrhagic, hypovolemic shock of burns, heat stroke and dehydration, septicaemic, neurogenic anaphylactic, and resuscitation of polytrauma, preloading and perioperative fluid maintenance of prolonged major surgery [1].

Comment 1

This is precisely when, where and how ARDS or MOVD/F occurs. It is an iatrogenic condition that complicates big bolus VO fluid therapy used for treating hypotension, with true or presumed volume deficit, that occurs only in hospitals most commonly on ICU but never in community.

Fact 2

The review [2] failed to recognize VO as causative insult of ARDS or MVOD/F because most of the reviewed articles never mentioned the volumetric status of patients. The first article on ARDS, that is also the first reference in the review, reported in 1967 by Ashbough et al at The Lancet [5], however, clearly documented VO of 12-14L in every case. Such VO was rarely mentioned in later reports while the condition changed its name from ARDS to MVOD/F to systemic inflammatory response syndrome (SIRS); demonstrating a major shift in understanding deviating too far away from, and thus totally missing, the most likely culprit of VO.

Comment 2

The most recent RCT, Clinical Trial Network, on which the comment article [1] was made aimed at the first 7 postoperative days. Thus it had already missed the event of big bolus VO given during surgery or resuscitation that induced and established ARDS in the first place! Limiting the review [2] to articles reported during the last 5 years is one reason for failure to recognize the relevance of VO in the pathogenesis of ARDS and MVOD/F, but there are many others.

Fact 3

Ever since fluid therapy had proved life-saving therapy for millions of polytrauma victims of the 2nd World War (WW2), the procedure was transferred into clinical practice later at mid 20th century with little or no further testing or verification, thus took with it all its overlooked complications.

Comment 3

The reports from WW2 and clinical practice from the fifties to seventies of the last century demonstrate that complications of fluid therapy recognized today as MVOD/F occurred then. The slogan of that era, that largely remains operative today, was: “Too much of a good thing must be a good thing”!? This is obviously and certainly wrong particularly as it applies to the goodness of water- while the right volume is vital for life, too much cause catastrophic flooding and drowning. The most important insult of VO and time of gain are rarely reported after the first report on ARDS [5]. It is important to identify not only VO quantity versus time (T) of gain but also fluid type and tonicity.

Fact 4

The cardiovascular volume of an adult is 5-6L with perhaps possible maximum vascular capacity of 7L that allow for physiological variation. Trying to fit 10-15L of fluid in 7L capacity container, spell fluid over causing such a big mess! Any infused bolus VO fluid that exceeds the cardiovascular capacity must leak out within minutes into the ISF (ISF) space. Some fluid pool in the third potential space of pleura, peritoneum and gut [1] and some fluid enter the intracellular space while the kidney is trying to execrate the surplus. The

vascular volume and tonicity are precisely regulated. When there is true vascular volume deficit most of the infused fluid stays intravascular topping up vascular volume to normal level, while an excess VO (Volume Loading) distributes within minutes between the vascular and ISF spaces with excess fluid spelling over into the third space after certain proportion of VO enter the intracellular space causing cell oedema.

Comment 4

While flooding of the ISF space manifest as trunk and limb oedema, the oedematous cell becomes ischaemic hypoxic and many disintegrate by hydrolysis manifesting with the clinical features of MVOD/F or SIRS. The flooded lung alveoli manifest as ARDS. The oedematous vital organ cells manifest as MVOD/F. The products of hydrolyzed cells leak its chemicals contents into the serum identified later as SIRS. Advances in ventilation and oxygen delivery at the lung, cardiovascular support and dialysis for renal support has incrementally prolonged survival and modified the clinical picture but failure at the capillary-ISF and cellular level remains as evidenced by the prevalence of morbidity and mortality of the MVOD/F.

Fact 5

A large bolus of overzealous liberal fluid VO is a constant insult in all cases of ARDS or MVOD/F while the listed causes in (Panel 1 in [2]) are the predisposing conditions or factors that vary from one case to another, which certainly have various severity and prognosis. To the mentioned list of predisposing conditions one may add prolonged major surgery and the polytrauma patients in whom ARDS or MVOD/F are also common.

Comment 5

The extra-vascular leakage of VO fluids into the ISF space is an internal flooding that cause the pathological torso and limb oedema affecting all cases of ARDS or MOVD/F commonly seen on ICU. The excess fluid is confirmed by increased body weight of 7-14 Kg. Whatever RCT may say, patients who die go to the mortuary with it and those who recover must lose it before discharge from the ICU or hospital. Any disbeliever should attend the postmortem examination of these cases. The eyes cannot miss the obvious oedema and flooding of internal organs and cavities, mental blindness is the problem that cannot be dealt with here.

Comment 5.1

The major concern and worry, is that most involved physicians do not consider such gross oedema pathological! It is even thought advantageous on the erroneous belief that overhydration irrigates tissues and cells! Such a view overlooks the obvious difference between irrigation and flooding that makes the difference between life and death. A subject with an excess of 7-14 Kg of body fluids causing ISF oedema, neither the oedema nor the subject can be considered as normal, otherwise he/she should not be on ICU. The most harmful effect of VO flooding ISF space, however, is not the visible subcutaneous oedema but is in fact the hidden cell oedema affecting the vital organs-revealed clearly on postmortem examination and also on modern CAT and MRI scans. Such cell oedema of vital organs manifest as features of MVOD/F syndrome such as comma, ARDS or respiratory or cardiac arrest, cardiac dysrhythmia or failure, acute renal failure, liver dysfunction or failure, also disturbances of serum contents and coagulopathies are common.

Fact 6

The clinical severity of ARDS and MVOD/F depends not only on fluid type and tonicity but also on VO quantity versus time (T) of gain; it is directly proportional to VO but inversely proportional to T [3].

Comment 6

For simplicity and practicality reasons, the complications of VO of therapeutic fluids used in clinical practice may be segregated into 2 groups based on the type of fluid: sodium-free fluid (Type 1) or VO1 and sodium-based fluid (Type 2) or VO2. Both groups induce ARDS or MVOD/F but have different pathological VO quantities and different haemo-dilution serum markers. There is minor variation among individual fluid members of each group. Large infusion or absorption of the irrigating fluids during the transurethral prostatectomy (TURP) surgery using 1.5% Glycine, Mannitol or Sorbitol, and 5% dextrose infusion and parentral nutrition are examples of VO1

fluid. A pathological VO1 induces the TURP syndrome with its characteristic acute dilutional hyponatraemia that ends up with the clinical manifestations of ARDS or MVOD/F [3]. Examples of VO2 fluids include normal saline, Hartmann's, Ringer's, plasma proteins, albumin, plasma substitutes and blood. These VO2 fluids have subtle serum markers and the pathological quantity is much larger. These VO2 fluids are used for volume expansion in treating hypotension of the mentioned predisposing conditions of ARDS or MVOD/F. Volumetric overload shocks have previously been reported [6,7].

Comment 6.1

On embarking on bolus volume expansion for the resuscitation of hypotension, it may be useful to consider the maximum capacitance of the vascular system of 7 L cannot be exceeded, and the maximum blood loss that is incompatible with life on arrival to a hospital is about its half or that equal plasma volume ≈ 3.5L. These figures represent 10% and 5% body weight. The latter figure with narrow deviation should limit the maximum volume to infuse after bleeding control, and still has the risk of pathological VO if all is given but not needed. It is also worth noting that of all shocks only the haemorrhagic has true blood volume deficit. A true fluid deficit also occurs in hypovolemic shock of burns, heat stroke and severe dehydration that require special careful assessment of the true deficit and meticulous replacement. Here the half century old argument on colloid versus crystalloids and the many RCT and systemic analysis on sodium versus albumin fluid evaluation (SAFE) may become pointless- as albumen does not work [4,11]. However, discounting the oncotic pressure of plasma proteins does not deny its useful nutrition and therapeutic value.

Cardiogenic shock has excess vascular volume and ISF oedema in which volume expansion is agreeably absolutely contra-indicated. All the remaining types of shock either have mal-distribution of fluid between the vascular and ISF spaces, or have micro-vascular dilatation while the normal vascular volume remains there. In all shocks, however, the exact pathology requires re-definition that differentiates irrigation from flooding of the ISF space in relation to cell oxygenation and viability. A suggested one is given later.

Fact 7

The authors of the article [1] stated that fluid preloading on induction of anaesthesia and the intraoperative insensible loss are highly overestimated and the liberal fluid infusions or volume expansion for combating hypotension are not evidence-based procedures.

Comment 7

I couldn't agree more with this statement. If it is brought to the attention of physicians involved in fluid management and resuscitation, and is implemented, a substantial reduction of cases of ARDS or MVOD/F will occur. The problem of chronic shortage of ICU beds will be resolved in days, many lives will be saved, morbidity, mortality and cost of ARDS will be substantially reduced, and no one should worry about losing his job because there is so much other work to be done.

Comment 7.1

The precise figures of therapeutic fluid replacement and physiological fluid challenge versus the pathological VO need quantification and definition. What is ambiguously referred to as conservative versus liberal approaches of fluid therapy [1,2], have wide personal and local variation. It is also of vital importance to recognize and identify the responses of therapeutic and physiological VO on one hand, and the paradoxical responses of pathological VO on the other, particularly its effect on the dynamic vascular pressures and renal function. It is documented that 3.5L of mostly VO1 causes paradoxical hypotension shock and acute renal failure (ARF) as features of the TURP syndrome that presents with essentially the same features of the MVOD/F syndrome [3]. These are exactly the opposite responses of physiological VO that are defined later.

Comment 7.2

The errors and misconception that mislead physicians, ICU and resuscitation team using massive liberal volume expansion in treating recognized shocks are deeply rooted. Erroneous concepts on vascular

volume-pressure relationship on the arterial and venous sides of circulation are identified below.

Error I

Every arterial hypotension is considered synonymous with hypovolemia or at least treated as such with volume expansion in every clinical case of shock, anaesthesia induction or perioperative maintenance!

Correction 1

Hypotension is not synonymous with hypovolemia. As mentioned above the cause of the primary recognized shock or hypotension must be differentiated. The difference between the therapeutic/ physiological VO regarding (quantity/ response) in contrast with the paradoxes of pathological VO regarding (quantity/ response) on arterial pressure and renal response must be identified and précised. Two paradoxical responses of pathological VO require recognition: one is inducing hypotension (VO/T) shock and the second is causing acute renal failure (ARF). The transition during overzealous volume expansion from the hypovolemic hypotension shock into the VO/T hypotension shock occurs seamlessly unnoticed and undetected by any monitoring until manifesting later on ICU with oedema increasing body weight of the ARDS or MVOD/F patients.

Error II

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

Correction II

The volume-pressure relationship particularly of vascular volume and arterial pressure is a limited line segment- beyond which the relation fails. Within limits, increasing vascular volume (physiological VO) increases arterial pressure but when such limit is exceeded (pathological VO) a paradoxical hypotension occurs. A similar VO paradox exists on the renal function; while physiological VO induces diuresis, a pathological VO causes anuria of ARF as part of the features of MVOD/F. These two paradoxes are not really new but hardly recognized or wrongly attributed to one of the recognized shocks.

Error III

The right atrium or central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) as monitoring parameters guiding fluid therapy are given value of 18 [2] to 22 mmhg as currently practiced on many ICU. Although the authors of both articles [1,2] stated that CVP and PCWP are unreliable and no longer being used, evidence from daily clinical practice and prevalence of ARDS and MOVD/F on ICU testify differently as it remain part of the definition given in panel 3 of [2]. The confounded error underlying the misconception of high positive CVP is related to deeply rooted error.

Correction III

The given figures of CVP and PCWP are erroneously too high and 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, then another bolus VO is given before the gross torso oedema and increase of 12-14 kg of body weight 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 mmhg. If we do not understand how Nature works we must faithfully imitate until reliable methods of monitoring fluid therapy are found.

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 or MVOD/F management should reconsider what is the physiological function of the arterial and venous pressures? And which pressure is responsible for what? The pathological ISF subcutaneous oedema is contrasted with the forces of the hypothesis that dictates capillary-ISF transfer on the causation of dropsy, proposed by Starling at the Lancet in 1886 [6]. The reason is that the forces on which this hypothesis is based govern the volume and pressure regulation of the vascular and ISF compartments, and subsequently cell viability. Being false, this hypothesis underlies most erroneous concepts on fluid therapy. Starling's hypothesis was made later into physiological law in error. It may be

realized that this is the major ERROR responsible for the current dilemma on ARDS or MOVD/F syndrome concealing its real patho-aetiology of VO [4].

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 straight line but also keeping high venous pressure and ISF tissue overhydrated are erroneously believed to enhance cell nourishment and oxygen delivery. This underlies the liberal volume expansion pumping in too much fluid that creates oedema, flooding and drowning of the ISF tissue, vital organs and cells! This is precisely the error underlying the pathological VO inducing ARDS and MVOD/F syndromes in current clinical practice.

Correction V

To assume the circulatory vascular system to be an all positive pressure system is quite simply wrong. In fact, there is a lot of negative physiological pressure under the skin of humans and animals in many areas and organs of the body that should be kept that way- as this is how it functions best. It is well known that the pleural spaces have negative pressure and the pressure in alveoli alternates. The venous pressure of normal subjects may swing around Zero, between positive +7 and negative -7 mmhg. The intracranial pressure is also negative. Thus the ISF space at subcutaneous tissues, most organs and parts of the body has a negative pressure of -7 mmHg that has been demonstrated and re-affirmed but neither considered nor satisfactorily explained.

Even in the lower limbs where venous pressure may have high positive value at erect posture, the veins are segmented by one way valves or pumped by muscular pump driving venous return towards the heart and keeping its dynamic venous pressure low. It is important to realize that not only fluids flow from high to low pressure in the venous system but it also from a negative pressure to a lower negative pressure! There is nothing that can explain the negative pressure of the ISF space with efficient rapid irrigation, not oedema, flooding and downing, except the negative energy phenomenon of the porous orifice (G) tube [4,11]. The only high positive pressure of the circulatory system is the arterial pressure and this seems to be so for a very good reason: it is the driving force for ejecting fluid through the capillary orifice creating the side negative energy pressure that drives the dynamic autonomous magnetic field-like fluid circulation between capillary lumen and surrounding tissues - keeping the ISF tissue pressure negative, appearing almost dry, while efficiently irrigated and oxygenated!

Question 1

What is volumetric overload?

Answer 1

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, Physiological VO should be adequate to cover the insensible fluid loss from fasting to end of surgery. In other words the safest maximum acute volume expansion should not exceed the capacitance of the vascular system by more than 1% BW. In situations where the loss is difficult to be accurately assessed, such as in polytrauma victims with internal cavity continuous bleeding and multiple fractures, it may be reasonably assessed in terms of maximum blood volume loss that is incompatible with life as basis for calculating volume replacement. In addition to clinical assessment, consider a normal recent body weight and calculate the real total blood and plasma volume of such patient as base line that is usually 10% and 5% BW, respectively.

To make it simple but accurate enough think of the vascular volume of ≈ 5-6L and capacitance of ≈ 7L of an adult. Its half equals the plasma volume of ≈ 3-3.5L that also approximately equals the daily fluid intake. Physiological bolus VO is about 1/3 of the plasma volume ≈ 1-1.167L/hour. This physiological VO plus the accurate therapeutic volume should be the maximum needed for resuscitation that should increase both the arterial blood pressure and urine output. If the patient does not respond, consider either a concealed blood loss continuing that need control while fluid replacement is being done, or other cause of the hypotension shock such as micro-vascular (Capillary

Sphincter) dilation or constriction of normo-volaemic patient, cardiac failure or a pathological VO/T has already occurred. Except for cases with internal blood loss, an acute increase in BW is perhaps the best available for detecting pathological VO. If acute volume expansion increased BW by more the 2% the risk of such pathological VO progressing into ARDS or MVOD/F is real. The type and tonicity of fluid used as well as its quantity and time of VO gain should also be considered.

Multiples of the bolus physiological VO in a normovolaemic subject may become pathological with increasing degree of severity. A pathological VO of 3.5L induces moderate ARDS or MVOD/F and certainly 7L is serious. These figures are accurate for VO2 fluids. For pure VO1 they are less by ≈1/3. A bolus means rapid infusion of VO within <1 hour. When the figures are transferred into percentage of body weight (BW), the plasma volume equals ≈ 3-3.5L (5% BW) of 70 kg adult. A physiological VO equals ≈ 1/3 of plasma volume ≈ 1-1.167L (≈ 1.67% BW). A pathological VO of ≈ 3%, 5% and 10% BW causes mild, moderate and severe ARDS or MVOD/F, respectively. The percentage figures apply to children and women also. Should you wish to make it more challenging, if the kidney remains functional, consider its maximum excretory ability in 1 hour, and subtract it from the gained VO, in order to determine the retained pathological VO. The next objective is to try to help the patient get rid of the retained VO surplus fluid within 24-48 hours while providing adequate ventilation and oxygenation, cardiac and vascular drug support, using diuretics and/or dialysis in cases of ARF. Extremes of age have poor tolerance to VO as do to dehydration and the related hormonal/ neuronal reflexes regulating vascular volume and tonicity under the stressful surgical conditions play an important role.

The type and tonicity of fluid affects clinical severity too. A pathological VO1 acutely loading the vascular system with 5% BW causes serious morbidity characterized by the acute dilution hyponatraemia. It induces paradoxical hypotension shock named as volumetric overload shocks and ARF [3]. This means that an acute change of the circulatory volume in either direction induces hypotension shock. The same VO of distilled water, still being used as irrigants for the TURP surgery at some parts of the World, is probably lethal via sequelae of intravascular haemolysis. The same quantity of VO2 fluids ≈ 5%BW may cause subtle pathological changes but VO2 of ≈ 7-14L (10-20%BW) is that observed in severe cases of ARDS or MVOD/F.

Volumetric Overload Shocks

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 hyponatremic shock [22] that was experimentally induced in dogs [8]. 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 [9,10]. 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 [5].

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 [9]. Volumetric overload *(figure 1)* was the only significant factor in causing the condition using multiple regression analysis (Table 1). The second clinical study involved a case series of 23 cases of the TURP syndrome manifesting as VOS1 [7-9] *(Figures 2)*. Volumetric overload quantity and type is shown in *(Figures 1 and 2)*. The first 3 cases of the case series 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 the dead.

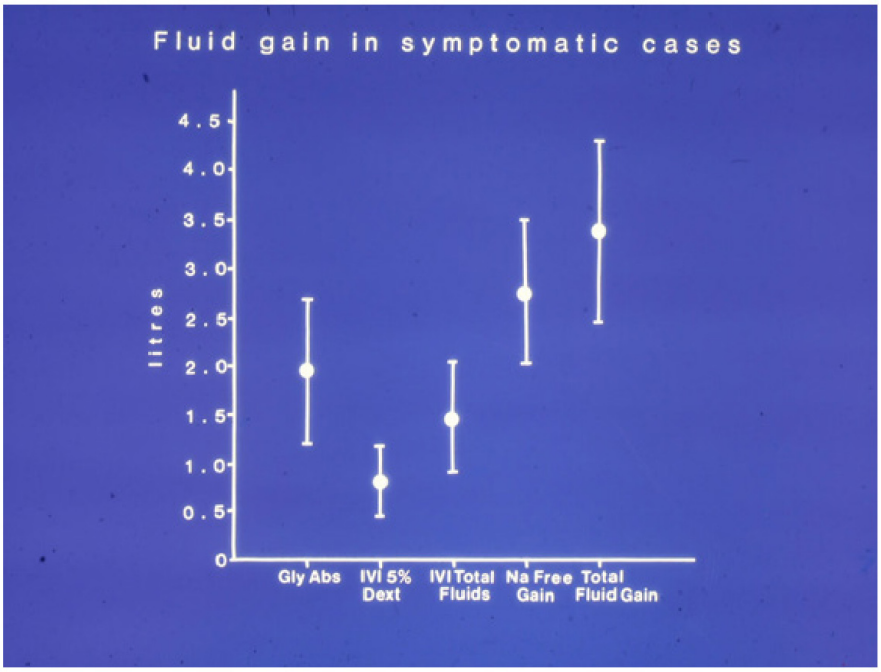

Figure 1. *shows the means and standard deviations of volumetric overload in 10 symptomatic patients presenting with shock and hyponatraemia among 100 consecutive patients during a prospective study om transurethral resection of the prostate. The fluids were of Glycine absorbed (Gly abs), intravenously infused 5% Dextrose (IVI Dext) Total IVI fluids, Total Sodium-free fluid gained (Na Free Gain) and total fluid gain in litres.*

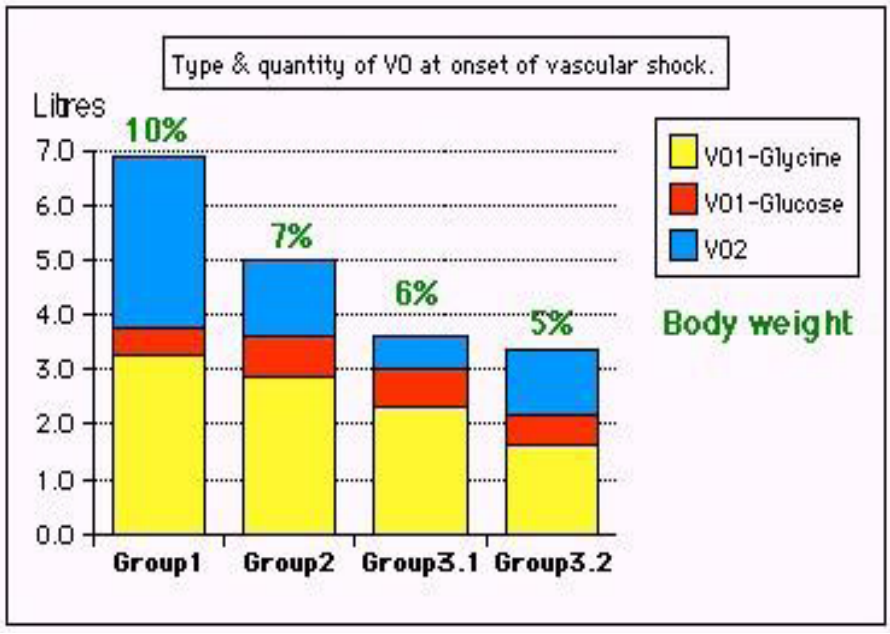

Figure 2. *shows volumetric overload (VO) quantity (in litres and as percent of body weight) and types of fluids. Group 1 was the 3 patients who died in the case series as they were misdiagnosed as one of the previously known shocks and treated with further volume expansion. Group 2 were 10 patients from the series who were correctly diagnosed as volumetric overload 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.*

Table 1. *shows the multiple regression analysis of total per-operative fluid gain, drop in measured serum osmolality (OsmM), sodium, albumin, Hb and increase in serum glycine occurring immediately post-operatively in relation to signs of the TURP syndrome. Volumetric gain and hypoosmolality are the only significant factors.*

Parameter	Value	Std. Err	Std. Value	T Value	P
Intercept			0.773		
Fluid Gain (l)	0.847	0.228	1.044	3.721	0.0001
OsmM (C_B)	0.033	00.014	-0.375	2.42	0.0212
Na+ (C_B)	0.095	0.049	0.616	1.95	0.0597
Alb (C_B)	0.062	0.087	0.239	0.713	0.4809
Hb (C_B)	-0.282	0.246	-0.368	1.149	0.2587
Glycine (C_B)	-4.973E-5	5.975E-5	-0.242	0.832	0.4112

The physical investigation involved studies of the hydrodynamics of the porous orifice (G) tube comparing it to that of Poiseuille's tube [4]. 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 (Figure 3). 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 [11]. It demonstrated that arterial pressure causes suction not filtration due to the effect of precapillary 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.

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 straight uniform brass tubes [14]. Latter evidence however demonstrated that the capillary is a porous narrow orifice (G) tube as it has a precapillary sphincter[12] and pores [13] that allow the passage of plasma proteins [4]. 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 [14] but there was no alternative at that time.

The hydrodynamics of the G tube [4] (Figure 3) 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 affecting 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.

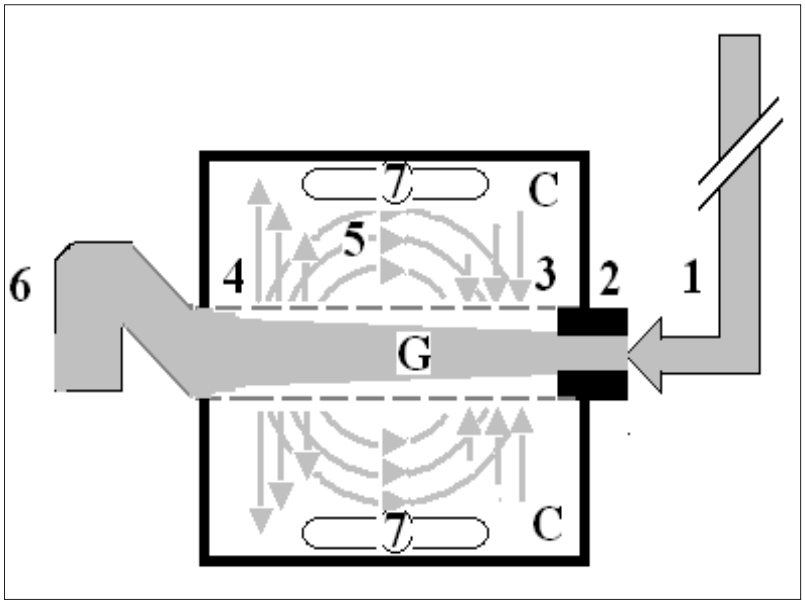

Figure 3. *shows diagram of the porous orifice (G) tube enclosed in chamber (C) based on several photographs demonstrating the magnetic field-like G-C circulation phenomenon. The proximal inflow (arterial) pressure (1) pushes fluid through the orifice (2) creating fluid jet in the lumen of the G tube. 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.*

Understanding the phenomenon of the porous orifice (G) tube may help to rectify the errors and misconceptions on intravenous fluid therapy, redefine recognized shock and identify the new VOS shocks that resolve the riddle of the ARDS or MVOD/F syndrome. No clinical RCT study will ever produce useful conclusions before the mentioned issues of facts and comments, errors and misconceptions are considered, stratified and rectified.

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