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Literature Review

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What is Misleading Physicians into Giving Too Much Fluid during Resuscitation of Shock and Surgery that Induces ARDS and/or AKI?

Ghanem AN[1*]

[1]Retired Consultant Urological Surgeon, Mansoura University, Faculty of Medicine, Egypt

Corresponding Author: **Ahmed N. Ghanem. MD, FRCS**
Address: Retired Consultant Urological Surgeon, Mansoura University, Faculty of Medicine, No 1, Jasmine Tower, President Mubarak Street, Mansoura 35511, Egypt; Tel: 00205022670 28; Mobile: 00201020883243; Email: anmghanem1@gmail.com

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Abstract

Introduction and Objective: Evidence demonstrates that there are many errors and misconceptions on fluid therapy. Starling's law underlies it all. This report gives the complete evidence that Starling's law is wrong on both forces and the correct replacement is hydrodynamic of the G tube. New physiological evidence is provided with clinical relevance and significance.

Material and Methods: The physics proof is based on G tube hydrodynamic. The physiological proof is based on a study of the hind limb of sheep: running plasma and later saline through the artery compared to that through the vein as regards the formation of oedema. The clinical significance is based on 2 studies one prospective and a 23 case series on volumetric overload shocks (VOS). The recent clinical studies on albumin and hydroxyethyl starch versus saline and also that on plasma proteins partly affirm that Starling's law is wrong. My physics and physiological research completes this evidence.

Results: Hydrodynamics of G tube showed that proximal, akin to arterial, pressure induces suction "absorption", not "filtration". In Poiseuille's tube side pressure is all positive causing filtration based on which Starling proposed his hypothesis. The physiological evidence proves that the capillary works as G tube not Poiseuille's tube: Oedema occurred when fluids are run through the vein but not through the artery. There was no difference using saline or plasma proteins, neither in physiological nor in clinical studies. The wrong Starling's law dictates the faulty rules on fluid therapy misleading physicians into giving too much fluid during shock resuscitation and surgery inducing VOS and ARDS.

Conclusion: Hydrodynamic of the G tube challenges the role attributed to arterial pressure as filtration force in Starling's law. A literature review shows that oncotic pressure does not work either. The new hydrodynamic of G tube is proposed to replace Starling's law which is wrong on both forces. The physiological proof and relevance to clinical importance on the pathogenesis of clinical syndromes are discussed.

Keywords

Capillary Physiology; Hydrodynamics; Starling's Law; Fluid Therapy; Shock, Hyponatramia; The Acute Respiratory Distress Syndrome (ARDS); AKI; Multiple Vital Organ Dysfunction /Failure (MVOD/F) Syndrome

Abbreviations

VO: Volumetric Overload; VOS: Volumetric Overload Shocks; VOS1: Volumetric Overload Shock, Type 1; VOS2: Volumetric Overload Shock, Type2; TURP: The Transurethral Resection of the Prostate; ARDS: The Adult Respiratory Distress Syndrome; MVOD/F: The Multiple Vital Organ Dysfunction /Failure Syndrome; AKI: Acute Kidney Injury; HN: Hyponatraemia; CVP: Central Venous Pressure; ISF: Interstitial Fluid; G Tube: The Porous Orifice Tube

There is evidence to suggest that physicians are misled to give too much fluid during the resuscitation of shock, acutely ill patients and patients undergoing prolonged major surgery[1]. The objective of this article is to answer the question of why this is happening and what is causing it. There are many errors and misconceptions on fluid therapy [1] that mislead physicians into giving too much fluid during resuscitation of shock and major prolonged surgery. This causes both severe and common morbidity and mortality among these patients. The morbidities include acute respiratory distress syndrome (ARDS) [2] and acute kidney injury (AKI) among the other manifestations of the multiple vital organ dysfunction/failure (MVOD/F) syndromes that include coma and cardiac and/or respiratory arrest [3,4].

My research has demonstrated that these syndromes are induced by volumetric overload (VO) presenting with volumetric overload shocks (VOS) [4-7] initially in theatre to anesthetists and surgeons during fluid resuscitation and later with MVOD/D syndrome coma, ARDS and/or AKI if the patient survived or with mortality. The errors and misconceptions on fluid therapy have been previously reported[1] underlying all of it is the faulty Starling's law [2].

Volumetric overload shocks (VOS) [4-7] are two types; VOS1 and VOS2, depending on the type of fluid inducing it: VOS1 is induced by a sodium-free fluid such as 5% Glucose and/or 1.5% Glycine used as irrigating fluid during the transurethral resection of the prostate (TURP) surgery. It is known in urology as the TURP syndrome [8,9] or hyponatremic shock [10].

This VOS1 is induced by 1.5% Glycine absorption and/or 5% glucose infusion of about 3.5-5 liters or >5% of bodyweight causing severe condition characterized by dilution hyponatremia (HN). Hyponatremia has 2 nadirs and 2 paradoxes [11] making it dynamic and illusive [12]. The 2 nadirs are the immediate drop of serum sodium level as a result of dilution of the extra-cellular fluid that occurs during or immediately after surgery. The second nadir is that occurring later, within 24 hours, after water shifts into the intracellular compartment causing spontaneous elevation of serum sodium level towards normal. Yet the clinical picture gets worse due to the generalized cellular oedema manifesting with MVOD/F syndrome [1,2]. Also using sodium-based saline solutions for treating VOS1 may correct serum sodium level but worsen volumetric overload inducing VOS2 and ARDS [1-7]. The 2 paradoxes are: A pathological volumetric overload induces hypotensive shock of VOS and AKI which is paradoxical to the physiological response of volume replacement that treats the known hypotensive shock and induces diuresis.

VOS1 currently has a lifesaving therapy of hypertonic sodium therapy (HST) of 5% NaCl or 8.4% NaCo3 [13]. It may present with cardiopulmonary arrest [3] or one or more of the other manifestations of MVOD/F syndrome- being the new name for ARDS. The manifestations include in addition to cardiac [3,4,14] and respiratory arrest [15] and VOS [5-7] that is usually mistaken for one of the recognized shocks [16]: coma, convulsion and paralysis [16-19], AKI [16] and hepatic dysfunction. It also causes coagulopathies and excessive bleeding at the surgical site [20]. VOS1 affects women too during the trans-cervical resection of the endometrium due to 1.5% Glycine absorption [17], and during Caesarean section due to excessive 5% Glucose infusion [18,19]. VOS is always mistaken for one of the recognized shocks [16] such as hemorrhagic and septic shocks thus it is wrongly treated with further volume expansion using sodium-based isotonic fluids. This induces VOS2 and

cardiopulmonary arrest that has no serum markers of HN and causes ARDS in patients who survive a little longer [1,2]. Multiple regression analysis has proved that volumetric overload is the most significant factor in causing the clinical picture of VOS (**Fig-1**, **Fig-2,** and **Table-1**) [8].

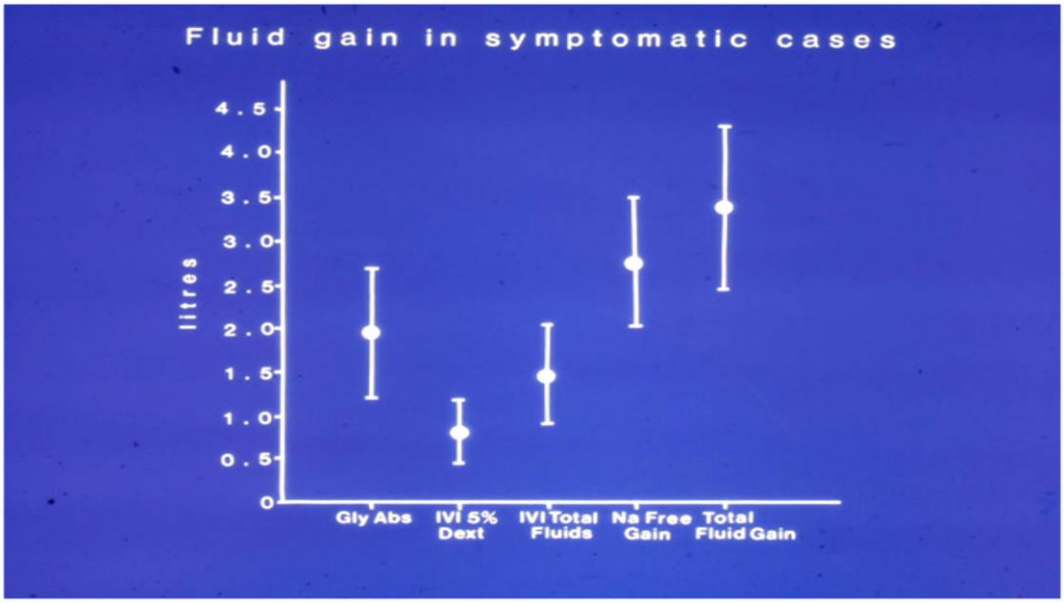

Fig-1:

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 on 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. (Reproduced with the permission of author and editor of BJU Int. from reference 8)

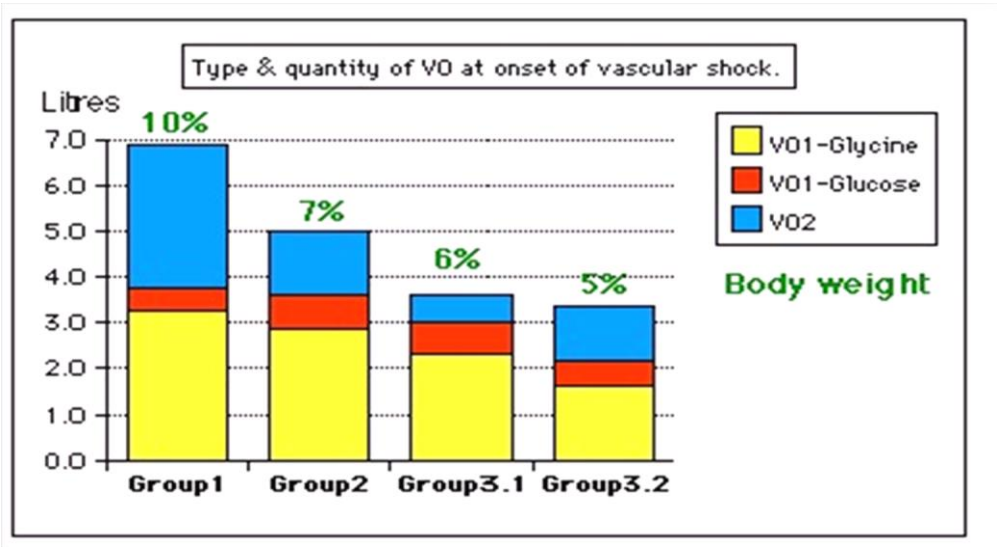

Fig-2:

Shows volumetric overload (VO) quantity (in litres and as % 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. (Reproduced with the permission of author from BHC open access journal reference 7)

Literature Review

Table-1: Multiple Regression Analysis of Total Per-Operative Fluid

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
Osmolality	0.033	0.014	-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)	-4.97E-05	5.98E-05	-0.242	0.832	0.4112

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. (Reproduced with the permission of author and editor of BJU Int. from reference 8).*

Volumetric overload shock type 2 (VOS2) [3-5] is induced by a massive infusion of sodium-based fluids such as Normal Saline, Hartmann, Plasma, Plasma substitutes of Hydroxyethyl Starch and Blood. VOS2 may complicate VOS1 or is induced by sodium-based fluid during fluid therapy for the resuscitation of shock and the critically ill patients and prolonged major surgery and presents with ARDS and/or AKI later [1,2]. The volumetric gain of 12-14 liters of sodium-based fluids reported in the first article on ARDS [21] which is the only article in the whole literature, other than the articles of mine referenced here, that documents the volume of retained fluid in ARDS. Discovery of VOS has resolved the puzzles of three conditions namely; the TURP syndrome, HN and ARDS. Not only the exact patho-aetiologies were identified but also curative therapy was found. These are real serial killers of hundreds of thousands of surgical and medical patients each year all over the world. Not only these most serious conditions preventable but also possibly curable when occurring inadvertently as iatrogenic complications of fluid therapy and treated promptly.

The reasons why Starling's law [22] is wrong [23,24] are summarized here:

1. The capillary has a pre-capillary sphincter as reported by Rhodin in 1967 [25] which makes it different from Poiseuille's tube of uniform diameter as my research demonstrated.
2. The capillary has a porous wall of intercellular slits that allow the passage of plasma proteins as shown by Karnoveski in 1967 [26]. Hence plasma proteins cannot exert an oncotic pressure in vivo.
3. The osmotic chemical composition of various body fluids is identical to plasma proteins as demonstrated by Hendry in 1962 [27], Hence oncotic pressure if it exists is too week and too slow to cause absorption.
4. The oncotic pressure of plasma proteins does not work as an absorption force either in physiology as proved by Hendry in 1962 [27] nor in clinical practice demonstrated by the Cochrane Injuries Group in 1998 [28].
5. More recent evidence demonstrates that both plasma proteins [28,29] and Hydroxyethyl Starch (HES) [30] vs Saline show no significant difference during the fluid infusion for the resuscitation of acutely ill patients and those undergoing major surgery.
6. Guyton and Coleman (1968) demonstrated that the interstitial fluid (ISF) space has a negative pressure [31] of -7 cm water and Calnan et al (1972) [32] showed that the lymph has the

same negative pressure. The pressure under the skin is negative. That cannot be explained by Starling's law.

7. Inadequacy in explaining the capillary–ISF transfer in many parts of the body as reported by Keele et al in 1982 [33], particularly vital organs, has previously called for reconsideration of Starling's hypothesis by Renkin in 1986 [34].
8. My physics and physiological research work has demonstrated that the hydrostatic or rather dynamic "arterial" pressure does not cause filtration across the wall of porous orifice (G) tube or capillary as proposed by Starling. It causes suction [23,24].
9. This pressure induces negative side pressure gradient along the G tube causing suction maximum near the inlet that turns positive maximum near the exit causing filtration as based on physics experiments [23] (**Fig-3**) and physiological research [24]. So both filtration and absorption are autonomous functions of the G tube. Venous pressure enhances filtration and causes oedema but arterial pressure does not cause absorption by suction.
10. The physiological study on the hind limb of sheep has completed the evidence that Starling's law is wrong as the capillary works as a G tube, not Poiseuille's tube [24].
11. Starling's law being wrong underlies all errors and misconceptions on fluid therapy misleading physicians into giving too much fluid during resuscitation of shock and the acutely ill patients and prolonged surgery inducing VOS [4-7] and causing ARDS [1,2].
12. Received thinking that elevating central venous pressure (CVP) is synonymous with elevating arterial pressure is prevailing in current clinical practice during fluid therapy for shock, the management of the acutely ill patient and

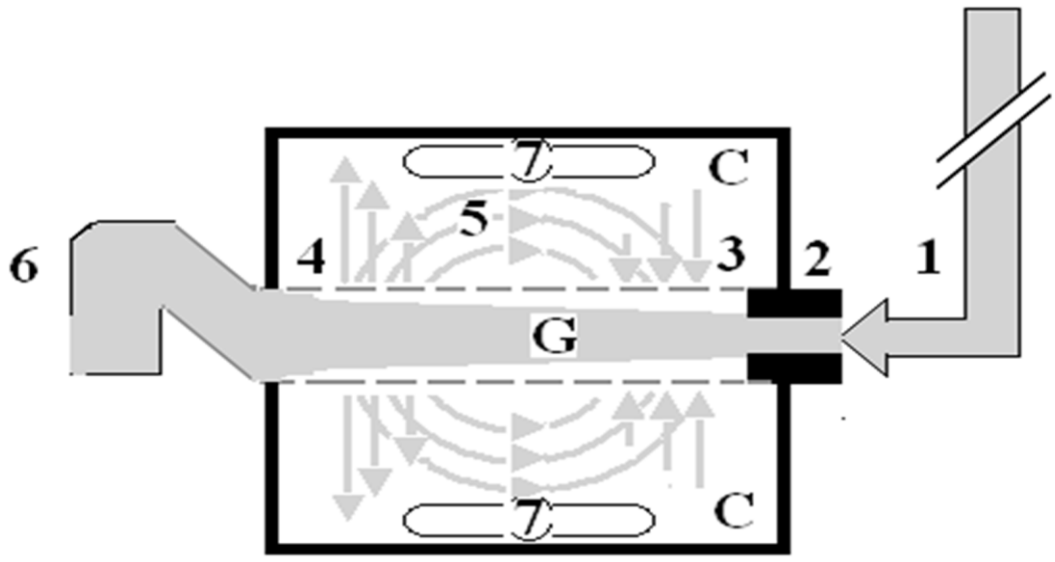

Fig-3:

Shows diagram of the porous orifice (G) tube enclosed in chamber (C) based on several photographs; some of it is shown here, 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. (Reproduced with the permission of author from BHC open access journal reference 23)

prolonged major surgery. This is undoubtedly correct during restoration therapy for hypovolemic and hemorrhagic shock, but vascular expansion or volumetric overload (VO) is a different issue as it induces VOS [4-7] causing ARDS [1,2].

13. Persistent attempts to elevate CVP up to levels of 18 to 22 cm water are common received practice, but wrong. The normal CVP is around 0 and most textbooks report a range of −7 to +7 cm water [33,35,36].
14. Clinical observations demonstrate that, in addition to the well-known effect of high venous pressure causing oedema, arterial hypertension has no such effect, if not the exact opposite. In clinical practice, although arterial hypertension is common, ISF oedema is unknown among its complications.
15. In the G–C model, a minor increase in DP increases fluid volume in chamber C around the G tube (**Fig-3**) reverting CP from negative to positive while slowing the G–C circulation. Increasing DP has a similar effect to decreasing PP on the G–C circulation and chamber pressure and volume.
16. The vascular expansion causes VOS [4-7]. There is no doubt that the erroneous Starling's law is responsible for the many errors and misconceptions prevailing on fluid therapy [1] for shock and the acutely ill patients and during prolonged major surgery which mislead physicians into giving too much fluid that induces VOS causing MVOD/F syndrome or (ARDS) [1,2] and AKI.

Further analytical review of the literature on ARDS has suspected liberal fluid use in resuscitation but never incriminated volumetric overload is causing ARDS or AKI. These authors [37] observed: "equal numbers of patients who appeared to have sepsis, severe sepsis, and septic shock but who had negative cultures. They had been prescribed empirical antibiotics for a median of 3 days. The cause of the systemic inflammatory response in these culture-negative populations is unknown, but they had similar morbidity and mortality rates as the respective culture-positive populations". This indeed makes sepsis and septic shock in the patho-aetiology of ARDS as innocent as the wolf in Josef' story as it may attack later doing its nasty work and inducing the markers of SIRS.

Also, these authors [38] stated in conclusion: "Although there was no significant difference in the primary outcome of 60-day mortality, the conservative strategy of fluid management improved lung function and shortened the duration of mechanical ventilation and intensive care without increasing non-pulmonary organ failures. These results support the use of a conservative strategy of fluid management in patients with acute lung injury."

The role of Starling's law played in this situation is merely hinted at in this article [39]. The authors of this article [40] also concluded: "Most deaths in the first 3 days after entry into the study could be attributed to the underlying illness or injury. The majority of late deaths were related to sepsis syndrome. Of the 22 patients with ARDS who died after 3 days, 16 (73%) met our criteria for sepsis syndrome. There was a six-fold increase in sepsis syndrome after ARDS compared with that in the control group ($p < 0.001$). When sepsis syndrome preceded the ARDS, the abdomen was the predominant source, but when sepsis syndrome occurred after the onset of ARDS there was usually a pulmonary source".

These authors ask an excellent question in the title of their report [41]. The answer was in conclusion: "These data support the concept that positive fluid balance per se is at least partially responsible for poor outcome in patients with pulmonary edema and defend the strategy of attempting to achieve a negative fluid balance if tolerated hemodynamically."

Findings

Physics, physiological and clinical evidence proves Starling's law is wrong. The literature review demonstrates oncotic pressure does not exist. Physics research demonstrates dynamic pressure induces suction, not filtration. Physiological evidence demonstrates that the capillary works as a G tube, not Poiseuille's tube. Hence Starling's law is wrong, yet it

dictates the faulty rules on fluid therapy. The correct replacement is hydrodynamic of the G tube.

Ethical Approval

Obtained for the original research [8]

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Author Contribution

All by the single author

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