

The Mechanisms of Action of the Non-Pneumatic Anti-Shock Garment

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INTRODUCTION

Globally, severe obstetric hemorrhage is the leading cause of maternal death, largely due to delays in accessing life-saving services such as surgery or blood transfusion¹⁻⁴. Effective, reliable means of stabilizing patients during delays in obtaining effective treatment would save many mothers' lives. This simplistic statement represents the premise underlying the use of the non-pneumatic anti-shock garment (NASG) in low resource settings. Preintervention phase/NASG phase studies in tertiary care facilities in Egypt and Nigeria have shown a 50% reduction in measured blood loss from a median of 400 ml to 200 ml ($p < 0.0001$); at the same time, mortality was reduced from 9% to 3.1% (RR 0.35, 95% CI 0.19–0.62)⁵. For details of clinical trials evaluating the NASG see Chapter 38. In this chapter, we discuss the mechanisms of action underlying the NASG, both what is known and the deficiencies where additional research is needed.

The NASG is an articulated neoprene and Velcro® first-aid compression device designed to reverse shock by shunting blood from the lower extremities and pelvis to the vital organs^{6,7}. The NASG is comprised of five articulated segments; the abdominal segment contains a foam ball for extra compression on the abdomen (Figure 1). It is *assumed* that the NASG increases circulating blood volume by compressing (and thus depleting) venous reservoirs in the abdomen and legs, and it is further *hypothesized* that blood flow in the pelvis and lower abdomen is diminished by the uterine compression ball. The NASG has had FDA 510K certification for over 20 years; however, until recently few studies evaluating the mechanisms underlying device effectiveness have been published. The work presented in this chapter is preliminary and far from complete, but it represents a thorough discussion of the ongoing efforts at obtaining a better understanding of how the NASG affects human physiology, particularly that of the pregnant/postpartum woman.

HISTORY OF ANTI-SHOCK GARMENTS

The use of anti-shock garments dates back to the early 1900s, when Dr George Crile created the first pneumatic suit to sustain blood pressure, decrease bleeding

and increase peripheral resistance⁷. In 1942, this was modified into what became the anti-Gravity suit, or G-suit, for the Army Air Corps in order to prevent syncope during rapid ascent⁷. During the Vietnam War, this same G-suit was used to stabilize patients suffering from shock and was modified from a full-body suit to a half-suit. As such, it became known as the Military/Medical® Anti-Shock Trousers (MAST suit) or pneumatic anti-shock garment (PASG)^{8,9}. Based on reported success in the field, this device was used more widely for emergency medicine and trauma patients in the 1970s^{10,11}. Recommendations for use of the garment and limited supportive anecdotal reports continued into the 1980s; however, by the late 1980s and into the 1990s several published studies raised questions regarding the efficacy and safety of the PASG¹²⁻¹⁶. A Cochrane database review in 2000 failed to find sufficient evidence to support the continued use of the garment, based in part on the increased mortality seen in patients with penetrating thoracic injuries¹⁷. Further, reports were published of side-effects, including compartment syndrome and ischemia, from over inflation^{12-16,18-21}.

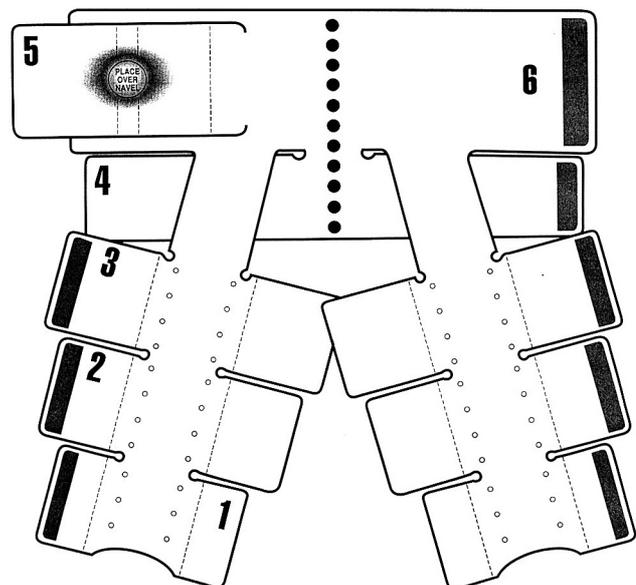


Figure 1 Schematic diagram of the non-pneumatic anti-shock garment

Despite these less than salutary findings when used in the area of general trauma, the PASG gained recognition as a possible first aid device for obstetric hemorrhage based on several case reports documenting favorable outcomes in cases of severe hemorrhage and shock²². Because obstetric hemorrhage results from blood loss from vessels that are branches of the internal iliac arteries (and ultimately the aorta), these findings are consistent with the thinking that the PASG has differential effectiveness depending on whether blood loss is from injuries below the waist or above²². The favorable findings of these case reports were further supported by studies of the hemodynamic impact of the PASG showing a significant decrease in aortic blood flow below the level of the renal arteries, suggesting that the device would be particularly useful for stemming uterine blood flow which is supplied by the internal iliac artery^{23,24}.

The NASG was adapted from the PASG by a team at the National Aeronautics and Space Administration (NASA). It was commercialized and is currently manufactured as the Non-Inflatable Anti-Shock Garment™ (ZOEX, Coloma, CA, USA). The first published report on NASG use for obstetric hemorrhage was a case series with six women in hypovolemic shock in Pakistan²⁵. The NASG has now been evaluated in comparative trials in Egypt^{26,27} and Nigeria^{5,28}, and qualitative studies have been conducted in Mexico²⁹ and Nigeria^{30,31}. An ongoing randomized clinical trial is being conducted in Zambia and Zimbabwe, with results expected in 2013. For details of the clinical trials see Chapter 38.

ANATOMY AND PHYSIOLOGY

Cardiovascular physiology of hypovolemic shock

Shock is a physiological state characterized by a decrease in tissue perfusion resulting in insufficient delivery of oxygen to the tissues. Deprivation of oxygen at the cellular level leads to a derangement of biochemical processes that result in systemic effects³². At the cellular level, the cell membrane ion pump begins to fail, leading to intracellular edema, leakage of intracellular contents into the extracellular space and changes in intracellular pH³³. These cellular changes then lead to alterations in the serum pH, endothelial dysfunction and the stimulation of inflammatory and anti-inflammatory cascades. If the tissue oxygen deprivation continues, the result is cellular death, end-organ damage, multisystem failure and ultimate demise³⁴.

Tissue perfusion is determined by cardiac output (stroke volume x heart rate) and systemic vascular resistance. Stroke volume is related to preload, myocardial contractility and afterload, while systemic vascular resistance is determined by vessel length and diameter and blood viscosity. Hypovolemic shock is a consequence of decreased preload due to intravascular volume loss, which in the case of obstetric hemorrhage results from severe uterine blood loss. The decrease in blood volume (decreased preload) results in a

diminished cardiac output, while the systemic vascular resistance increases initially to compensate and maintain perfusion.

Shock progresses along a physiological continuum that begins with preshock when the patient is compensating for the blood loss through increased heart rate, peripheral vasoconstriction and minimal changes to systemic vascular resistance³⁵. As the situation progresses, however, the compensatory mechanisms become overwhelmed, and the patient experiences tachycardia, dyspnea, restlessness, metabolic acidosis and oliguria. If shock continues to progress, organ damage may become irreversible with renal failure, acidemia and severe alterations in cellular metabolism. At this stage, the patient may rapidly evolve from an agitated to an obtunded and, finally, to a comatose state. It is therefore axiomatic that early identification of hypovolemic shock with cessation of bleeding, replacement of intravascular volume and supportive measures (such as oxygen supplementation) are critical to preventing end-organ damage and death.

Anatomy of blood flow to the pelvis

The descending aorta bifurcates into the right and left common iliac arteries at the level of the fourth lumbar vertebrae. The common iliac then divides into the internal (sometimes called the hypogastric) and external iliac arteries. The external iliac artery provides the blood supply primarily to the lower extremities as the femoral arteries, while the internal iliac supplies the walls and internal organs of the pelvis, the gluteal muscles and the medial compartment of the thigh. The uterine blood supply is derived primarily from the uterine artery, which is a branch of the internal iliac artery. About 15–20% of the uterine blood supply comes from the ovarian artery, which branches directly from the aorta just below the renal arteries. The uterine artery anastomoses the ovarian artery superiorly and the vaginal artery inferiorly also supplying a portion of the blood to the ovary and vagina, respectively. In hypovolemic shock due to uterine atony, if uterotonics and tamponade (either balloon or manual) (see chapters in Section 8) fail to control hemorrhage, the next step generally involves surgical intervention for vessel ligation (uterine, ovarian or internal iliac) or to place uterine compression sutures (B-Lynch or one of its modifications see Chapter 51). The O'Leary stitch is performed by ligating the ascending branch of the uterine artery; in contrast, the internal iliac artery ligation involves placing a stitch just after the posterior division has branched off (see Chapters 52 and 53). Both result in cessation of blood flow and a cessation of the arterial pulse pressure beyond the point of ligation.

Urban *et al.* have evaluated blood flow to the uterus during labor and delivery using Multigate spectral Doppler analysis and have demonstrated that uterine contractions following delivery result in absent flow in the arcuate artery (Chapter 12).

THEORETICAL MODEL OF NON-PNEUMATIC ANTI-SHOCK GARMENT FUNCTION

At least two main theoretical mechanisms of action underlie the effectiveness of the NASG. The first involves the shunting of blood from the lower extremities and pelvis back to the central circulation in order to improve perfusion of vital organs. The second involves the pressure exerted by the abdominal compression ball onto the uterus and surrounding vasculature in order to decrease blood flow to the pelvis and diminish uterine blood loss. A model of these proposed mechanisms of action is shown in Figure 2.

Physical laws

Circumferential compression of the abdomen and lower extremities, leading to a reduction in total vascular volume, is thought to be the main mechanism accounting for ASG efficacy^{15,27}. Preload, peripheral resistance and cardiac output are increased as a result of the expansion of the central circulation. Three laws of physics underlie these changes. First, Poiseuille's law ($F = (P1 - P2) R^4/8NL$) states that the flow rate (F) through a blood vessel is related to the vessel's radius (R) to the 4th power, the length of the vessel (L) and to viscosity (N), where P1 is the entrance pressure and P2 is the exit pressure. Therefore, reduction in the vessel radius should lead to exponential reductions in blood flow. Second, Laplace's law ($T = PR$) relates the tension (T) across a blood vessel to the vessel radius (R) and the transmural pressure (P). External pressure exerted on the lower body by the ASG reduces the transmural pressure and the radius of the vessel, thereby reducing both tension and blood flow. Finally, Bernoulli's principle [$Q = (AP + 2V)/E$] describes how the rate of bleeding (Q) depends on the area of the torn vessel wall (A) and the transmural pressure (P), where E is the density of blood and V is the velocity of blood flow (Figure 3). External pressure from the ASG compresses vessels, leading to diminished vascular volume in the compressed area, an exponential decrease in flow and, ultimately, reduced blood loss^{15,27}.

PHYSIOLOGIC STUDIES OF THE PNEUMATIC ANTI-SHOCK GARMENT

Animal studies

Several animal studies have demonstrated decreased bleeding, increased systolic blood pressure and improved survival after placement of a PASG/sleeve. The first study, a case series using eight dogs treated with a pneumatic abdominal sleeve after having had their intra-abdominal aorta transected, had a sustained mean systolic blood pressure of 74 mmHg. After removal, six of eight dogs died within 5 minutes, but two dogs survived 30 and 40 minutes and showed sealing of the aortic incision³⁶. Subsequently, in 1969 a comparative study was performed using 16 dogs (eight controls, eight PASG) that had undergone lacerations

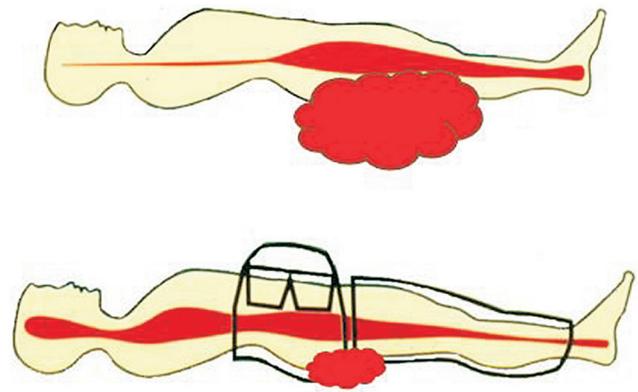


Figure 2 The NASG reverses the effects of shock by decreasing the container of the circulatory system as it compresses the lower extremities and abdomen. This increases the circulating volume in the uncompressed upper body. Thus, there is more blood circulating to the brain, heart and lungs, elevating blood pressure and increasing preload and cardiac output. Further, the circumferential pressure of the tight neoprene and the additional pressure exerted by the abdominal compression ball decreases the radius of the blood vessels in the pelvis; decreasing blood flow and reducing uterine blood loss

<p>Poiseuille's Law</p> <p>$F = (P1-P2) R^4/8N*L$</p> <p><i>F, flow; P1, entrance pressure; P2, exit pressure; R, radius; N, viscosity; L, length</i></p>
<p>Laplace's Law</p> <p>$T = P*R$</p> <p><i>T, tension inside blood vessel; P, transmural pressure; R, vessel radius</i></p>
<p>Bernoulli's Principle</p> <p>$Q = (A*P + 2V)/E$</p> <p><i>Q, rate of leakage; A, area of laceration/tear/opening; P, transmural pressure; E, density of blood; V, speed or velocity of blood flow</i></p>

Figure 3 Laws and principles governing the mechanisms of action underlying ASGs

of the iliac artery. All controls died within minutes; however, the dogs with the PASG survived until it was deflated, after which 75% expired within 5 minutes³⁷.

Subsequently, another group of researchers studied 30 rats with lethal hepatic and vena caval injury. Animals were allocated as follows: five controls, five with PASG alone, ten with saline infusion alone and ten with PASG and saline infusion. The PASG group demonstrated improved median survival compared to controls (120 min vs. 10 min). The group that received saline infusion alone showed no survival improvement, and fulminant pulmonary edema developed in 90% of the rats that received both the PASG and saline³⁸.

In a study of 12 dogs (six controls, six PASG) with splenic crush injuries, the PASG group effectively

sustained systolic blood pressure after 1 hour (100 mmHg vs. 0 mmHg in controls), survived twice as long as controls (2 h vs. <1 h) and bled significantly less (1.6 ml/min vs. 9.4 ml/min)³⁹.

The effect of the PASG on the cerebral function of 29 rats with severe hepatic injury was examined in another murine study. The PASG prolonged the time before the EEG amplitude began to decrease, the time during which a sensory response could be observed and increased survival time⁴⁰.

The hemodynamic effect of the PASG was studied using 20 anesthetized dogs (10 controls and 10 PASG) with hemorrhagic hypotension⁴¹. Carotid artery blood flow increased by 50% and femoral artery decreased tenfold in the PASG group; this was accompanied by a transient increase in cardiac output (2.4 l/min to 2.7 l/min; $p < 0.05$), which later fell to 1.9 l/min. The authors concluded that an initial increase in cardiac output due to compression of the venous system was followed by an emptying of the blood into the central circulation; however, this combination of events later led to a reduction of cardiac output due to further venous compression and an increase in afterload, without an increase in preload.

Subsequently, using three groups of piglets, it was shown that with a small (2.5 mm) injury to the descending aorta, hemorrhage and mortality were increased with the PASG⁴². In group 1, the animals did not have the garment applied and 100% survived; the hemorrhage rate was 22.5 ml/min, and bleeding stopped after 18–24 min. In group 2, a PASG was inflated to maintain 15 torr below the piglet's normal baseline carotid artery pressure; in this group, survival was 50% and the animals bled at a rate of 32.5 ml/min, stopping after 26–35 min. In the third group, the PASG was inflated to maintain the normal baseline pressure of the carotid artery. The pigs bled at 107.5 ml/min and none survived, with expiration after 10–18 min being the norm. This finding led the authors to conclude that with thoracic injury, PASG inflation increases mortality and hemorrhage. Their conclusion is not surprising given the discussion presented above showing that its use is more effective when the source of the blood loss was lower in the trunk.

In summary, animal studies of the PASG to date have demonstrated significantly decreased bleeding and increased survival time after aortic or internal iliac laceration, and lethal hepatic or vena cava injury; however, when injuries occurred in the thoracic region, the PASG resulted in increased mortality. The PASG has been shown in animal studies to decrease femoral artery blood flow (10 times), increase carotid artery blood flow (50%) and transiently increase cardiac output as well as improve cerebral function.

Human studies

The hemodynamic effects of PASGs have been examined in several human studies. In 1981, Gaffney *et al.* demonstrated with 10 healthy normovolemic male

patients who were not bleeding placed in the supine position that the PASG raised blood pressure and increased peripheral resistance but slightly decreased cardiac output and stroke volume⁴³. When these patients were examined with a 60-degree head up tilt (which leads to venous pooling in the lower extremities and more closely approximates hypovolemia), PASG application induced a 30% increase in cardiac output, a 52% increase in stroke volume and a 40% increase in total peripheral resistance.

Two dimensional echo was used to evaluate the effect of the PASG on end diastolic volume, stroke volume, cardiac output and blood pressure in eight supine healthy non-bleeding males using two different inflation protocols (50 and 100 mmHg)⁴⁴. Both protocols resulted in a rise in end diastolic volume and blood pressure. In the 50 mmHg protocol, the stroke volume and end diastolic volume decreased over time, whereas with the 100 mmHg protocol, the cardiac output was increased and maintained, likely through the mechanism of increased peripheral resistance. A second study by the same research group reported that the optimal inflation sequence to produce the greatest increase in end diastolic volume, stroke volume and cardiac output was to inflate the legs simultaneously, followed by the abdominal segment⁴⁵.

The effects of different pressure levels (2, 4 and 6 psi) on 10 healthy male volunteers in supine and standing position were also investigated⁴⁶. Again, while supine, the men experienced increased blood pressure with all three pressures, but cardiac output and end diastolic volume did not increase. In the standing protocol, however, mean arterial pressure, end diastolic volume, stroke volume and cardiac output rose at all three inflation pressures ($p < 0.05$). This observation suggests that increases in blood pressure are caused by increased cardiac preload and cardiac output in the standing position, which more closely approximates hypovolemia, and suggests utility of using the PASG for hypovolemic patients. This study further demonstrated that the effects of the PASG differ depending on the amount of pressure applied/level of inflation.

More recently, the effect of the PASG inflated to 90 mmHg was studied in 10 healthy adults²³. Cardiac output and blood flow in several major arteries including the left carotid, left subclavian, superior mesenteric, left renal and distal aorta were measured. The authors demonstrated no change in cardiac output (5.45 vs. 5.83 l/min; $p = 0.26$), or left subclavian or left carotid blood flow, whereas aortic blood flow distal to the renal artery was markedly decreased in all subjects (1.01 vs. 0.11 l/min, $p < 0.001$). The authors concluded that the PASG has a dramatic effect on aortic blood flow distal to the renal arteries, but does not significantly affect flow above that point, and suggested that the garment may result in decrease in bleeding from injuries distal to this point (iliac, pelvic and lower extremity vessels) (Figure 4).

A subsequent case documenting use of the PASG in a woman with pelvic trauma supports the findings of

the study reported above²⁴. The patient presented in a severe state of shock with a Glasgow coma scale of 6, systolic blood pressure of 60 mmHg and pulse of 80 beats/min with suspicion of pneumothorax. The PASG was inflated to a pressure of 60 mmHg in the extremities and 50 mmHg abdominally. After placement, blood pressure rose to 72 mmHg and her pulse became 121 bpm. The patient then was taken to angiography for possible embolization. The PASG was deflated to place the embolization catheters, and the internal iliac artery visualized. Once the abdominal segment of the PASG was re-inflated the internal iliac was no longer visualized on angiography, and blood flow through the vessel had effectively stopped. The patient then received embolization to control the hemorrhage permanently, along with multiple blood products to correct her deficiencies²⁴.

The studies of the PASG in human subjects to date have documented increased blood pressure, but have found mixed results on the effect of the PASG on cardiac output, stroke volume and end diastolic volume. These parameters appear to vary with inflation pressure and/or patient position (supine versus standing or 60-degree head tilt). The PASG significantly decreases blood flow in the distal aorta.

External aortic compression device

An external abdominal compression device, made of a strong metal spring that is cylindrical in shape and covered with leather, also has been studied for use in PPH^{47,48} (Figure 5). The device is set to exert 103.5 mmHg/cm² and is placed just above the compressed fundus over the umbilicus with the objective of compressing the distal aorta. Use of this compression device reduces the time to cessation of bleeding (36.8 vs. 118.6 min; $p < 0.001$), the number of blood transfusions (200 vs. 302 units) and the amount of uterotonics used ($p < 0.001$)⁴⁷. The investigators also studied femoral artery blood flow using Doppler velocimetry analysis with the device in place, showing that flow to the lower extremities is reduced, but remains sufficient to maintain tissue perfusion⁴⁸.

PHYSIOLOGIC STUDIES OF NON-PNEUMATIC ANTI-SHOCK GARMENT

For each of the studies described below, IRB approval was obtained from the University of California, Los Angeles, and/or the University of California, San Francisco and all participants/volunteers underwent an informed consent process.

Measured blood loss

Data from the NASG clinical trials conducted in Egypt and Nigeria demonstrated a significantly diminished blood loss (50%) with application of the NASG in pre-intervention phase/NASG intervention phase studies ($p < 0.0001$)⁵. A further analysis of Egyptian women with uterine atony revealed that even

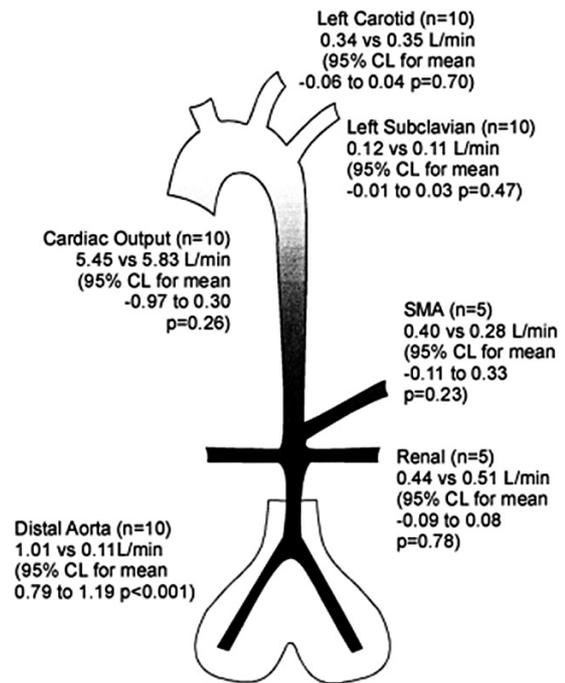


Figure 4 A diagram of blood flow before and after ASG inflation. CL, confidence limit; SMA, superior mesenteric artery. From Hauswald M, Greene R. Regional blood flow after pneumatic anti-shock garment inflation. *Prehospital Emergency Care* 2003;7:225–8, with permission

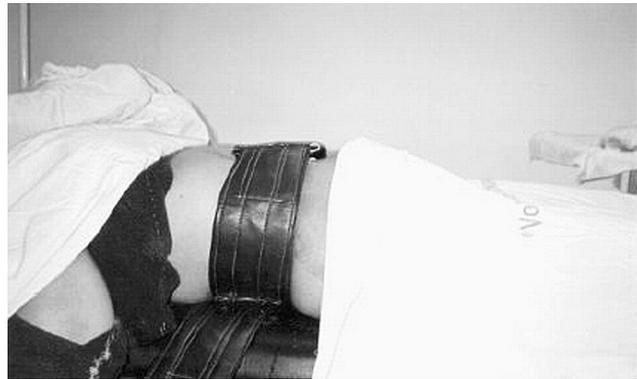


Figure 5 External aortic compression device. From Soltan *et al.* Assessing changes in flow velocimetry and clinical outcome following use of an external aortic compression device in women with postpartum hemorrhage. *Int J Gynecol Obstet* 2010;110:257–61, with permission

after controlling for the amount of administered uterotonics, women treated with the NASG had 303 ml less measured blood loss (299 ml) compared with the women who did not have the NASG available (602 ml)²⁷.

Shock index

The time to recovery of a normal pulse was faster for women with hypovolemic shock in the NASG-intervention phase (90 min) than for women in the pre-intervention phase (180 min) in Egypt²⁶. This difference also held when the pulse at study entry was controlled for²⁶. The shock index (SI) is a better

clinical indicator of hypovolemia than either the pulse or the blood pressure alone, because it simultaneously accounts for both pulse (P) and systolic blood pressure (SBP). The formula⁴⁹ for the SI is $SI = P/SBP$. A higher shock index is associated with a greater risk of severe morbidity and mortality. When the data from the Egyptian NASG study were analysed, the median recovery times for the SI were significantly shorter in the NASG-intervention phase (75 min) than in the pre-intervention phase (120 min) (log rank 8.99, $p = 0.003$); this effect persisted even after stratifying for SI at study entry as well as blood transfusion and IV fluids received²⁶ (Figure 6).

External abdominal pressure

The effect of the NASG on the pressure exerted on the external abdominal wall underneath the NASG abdominal compression ball was studied in 10 healthy non-pregnant, non-postpartum female volunteers⁵⁰. No participant reported any side-effects during NASG application and vital signs remained stable throughout. Mean pressures were low at baseline (1.1 mmHg, SD 1.9), with a significant rise upon full application after 5 min (66.6 mmHg, SD 11.2), and a rapid return to near baseline levels upon complete removal (-1.9 mmHg, SD 3.8). Pressure at full application after 5 min was significantly greater than pressure immediately before application (Wilcoxon matched-pairs signed-rank test; $p = 0.005$) and upon removal ($p < 0.001$) (Figure 7)⁵⁰.

The effect of body mass index and applier strength

Ten healthy non-pregnant, non-postpartum volunteers with varied body mass indexes (BMIs) were evaluated in a separate study to evaluate the effect of BMI and applier strength during application⁵⁰. Average age of study participants was 33 years, the majority were nulligravid (8/10), and two had delivered two children each. Mean BMI by category were as follows: three underweight (mean BMI 18.3), four normal weight (mean BMI 21.0) and three overweight (mean BMI 30.3). Two appliers of different self-reported strength (one strong and one weak) were recruited to apply the NASG to each of the volunteers. There were a total of 20 applications, with each volunteer having a 'strong' and a 'weak' application of the NASG.

For all participants, application of the NASG resulted in a significant increase in pressure at the level of the abdominal wall. There were no changes in vital signs with application of the NASG and no reported side-effects. A high degree of correlation existed between the pressure generated immediately after application and after 5 min with both strong (Spearman correlation 0.963, $p = 0.001$) and weak appliers (Spearman correlation 0.854, $p = 0.002$). Application of the NASG by the strong applier versus the weak applier for all three BMI groups resulted in higher mean pressure (Figure 8). The difference between the pressure generated by a strong applier in an

underweight patient and a weak applier in an overweight patient was statistically significant (Wilcoxon rank sum test; $p = 0.05$)⁵⁰.

An inverse relationship existed between pressure and BMI, which was statistically significant for

Cox regression results for the effects of study group on shock index recovery time, controlling for initial SI value and other resuscitative measures						
	B	Wald	Sig.	Exp(B)	95.0% CI for Exp(B)	
					Lower	Upper
Blood transfusion (n = 222)						
NASG	0.651	19.337	0.000	1.918	1.435	2.563
Initial SI value	-1.199	15.809	0.000	0.301	0.167	0.544
Blood transfusion for resuscitation	0.856	26.131	0.000	2.353	1.695	3.266
Volume of IV fluids given in the first hour (n = 196)						
NASG	0.454	8.519	0.004	1.575	1.161	2.136
Initial SI value	-1.841	37.367	0.000	0.159	0.088	0.286
More than >1000 ml of IV fluids in first hour	0.154	0.829	0.363	1.167	0.837	1.625

Figure 6 Egyptian NASG study data, the median recovery times for the shock index (SI) were significantly shorter in the NASG-intervention phase (75 min) than in the pre-intervention phase (120 min) (log rank 8.99, $p = 0.003$); this effect persisted even after stratifying for SI at study entry as well as blood transfusion and IV fluids received. B, beta (the estimated regression coefficient); Wald, Wald statistic; Sig., significance of the Wald statistic; Exp(B), predicted change in the hazard for a unit increase in the predictor. From Miller *et al.* Use of the non-pneumatic anti-shock garment (NASG) to reduce blood loss and time to recovery from shock for women with obstetric haemorrhage in Egypt. *Global Public Health J* 2007;2;110–24, with permission

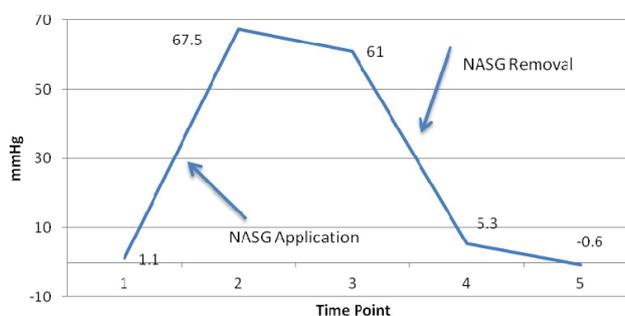


Figure 7 The effect of NASG on mean external abdominal wall pressure ($n = 10$)

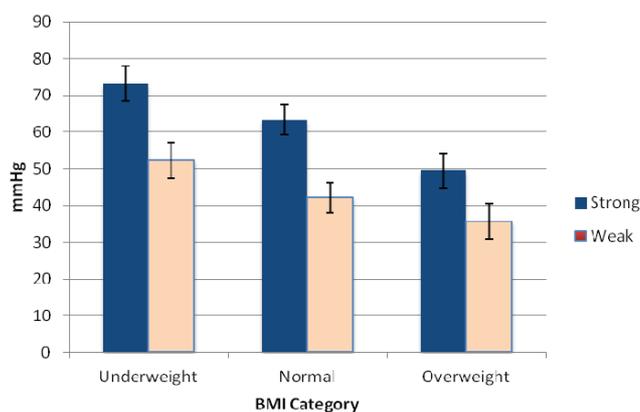


Figure 8 Mean pressure during NASG application by strong and weak appliers for each BMI category with standard error bars ($n = 10$)

the strong applier (Spearman correlation -0.905 , $p = 0.0003$), but not significant for the weak applier (Spearman correlation -0.232 , $p = 0.5182$). Placement of the NASG abdominal segment for 5 min resulted in a rapid rise in mean pressure on the external abdomen below the NASG abdominal compression ball in both the strong and weak applier groups (see Figure 4). The mean pressure generated by the strong applier was significantly greater than that generated by the weak applier (ANOVA; $p < 0.001$) (Figure 9). Pressure rapidly returned to baseline after removal of the NASG. Vital signs in these euvolemic female volunteers did not change with NASG application⁵⁰.

Pelvic blood flow

Because NASG users have a decrease in uterine bleeding after garment application, investigators considered how the NASG affects blood flow to the uterus specifically. Two recent studies investigated the effect of the NASG on lower abdominal or pelvic blood flow.

Hauswald *et al.* studied the effect of the NASG on distal aortic blood flow in 12 healthy adults (male or female not-specified)⁵¹. Using an Acuson Sequoia 512 Ultrasound and 4VI probe operating at 2–3 MHz (Siemens, Mountain View, CA, USA), measurements were obtained of heart rate, apparent artery diameter, Doppler-to-vessel angle and blood flow velocity at the abdominal aorta below the superior mesenteric artery (SMA). These data then were used to calculate flow rate (volume per time). Placement of the NASG resulted in a mean decrease in blood flow in the distal aorta of 33% or 0.65 l/min. This result then was compared to an improvised pneumatic anti-shock device made out of three bicycle tubes and sheets, which decreased flow by 56% or 1.11 l/min.

A study by Lester *et al.* examined the impact of the NASG on internal iliac resistive indices (RI) of healthy postpartum volunteers⁵². The RI is defined as the peak of systole divided by the sum of systole (S) and diastole (D): $RI = S/(S + D)$. A higher RI is correlated with decreased blood flow to a given vessel. A value less than 1.0 indicates forward flow, whereas a value of greater or equal to 1.0 indicates absent or reverse flow. All 10 patients evaluated in this study had delivered vaginally at term without complications. The majority (9/10) had received prophylactic IV oxytocin after delivery; one did not. The mean time from delivery to study inclusion was 12 h (range 2–18 h). Mean maternal age was 25 (range 18–37), and the patients had delivered an average of 2.4 babies (range 1–6). The majority were normal weight; none were underweight, and four were overweight.

The median internal iliac RI was evaluated using transabdominal Doppler ultrasound at nine time points before, during and after application of the NASG. Little change was observed in RI from baseline (0.83, SD 0.11) with application of leg panels alone (0.84, SD 0.12). When the abdominal panel was applied, however, the median value rose significantly (1.05, SD 0.15) and stayed elevated after full application for

10 min (1.00, SD 0.15). The RI rapidly returned to baseline with removal of the abdominal segment (0.82, SD 0.04), and remained low and near baseline after the removal of the entire garment (0.81, SD 0.11). There was a significant change in RI from baseline to full application (Wilcoxon matched-pairs signed-rank test; $p = 0.02$), as depicted in Figure 10. Vital signs in these euvolemic women remained stable throughout the application with little change noted in any of the parameters⁵⁰.

Several methods are available for analysing Doppler blood flow including flow volume or velocity measurement, resistance indices and waveform analysis⁵³. Flow volume analysis most closely approximates true blood flow; however, it is difficult to perform and prone to error, as accurate measurement is dependent on the angle of insonation, vessel diameter measurement and vessel tortuosity. Most ultrasound machines used in routine obstetrics are not able to calculate flow volume due to the high analytic requirements of these calculations. Resistance indices are indirect measures of flow volume; however, they are angle independent and are considered to be useful for estimating blood flow in vessels distal to the point of the examination. One drawback of RI calculation is that it may not be as accurate in cases when blood flow is not continuous throughout the cardiac cycle. Waveform analysis is more complicated; however, it may provide a more accurate estimate of blood flow in conditions of

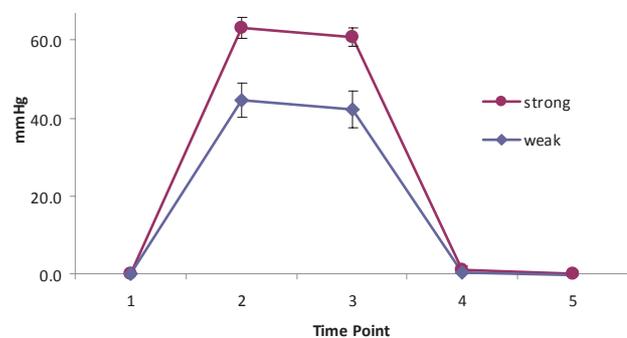


Figure 9 The effect of applier strength on mean pressure with NASG application ($n = 10$)

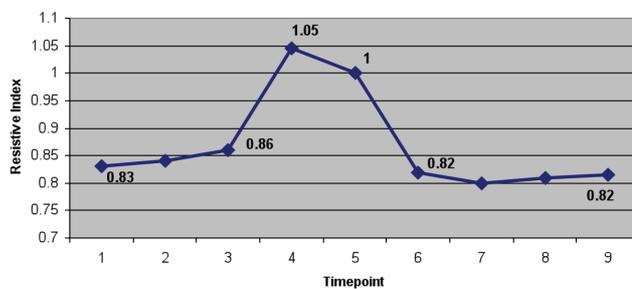


Figure 10 Median internal iliac resistive index with application of NASG. (Timepoint 1 is baseline, 2 is application of the leg segments, Timepoint 4 is full application of the NASG. Timepoint 6 represents removal of the abdominal panel. Timepoint 8 is after full removal of the garment.) Lester *et al.* Impact of the non-pneumatic antishock garment on pelvic blood flow in healthy postpartum women. *Am J Obstet Gynecol* 2011;204:409.e1–5

non-continuous blood flow during the cardiac cycle⁵³. In the study cited above, the blood flow to the pelvis was measured transabdominally using Doppler ultrasound. Due to the location of the NASGs abdominal/pelvic segment and uterine compression ball in relationship to where the transabdominal ultrasound probe should be placed to image the uterine artery, an accurate measurement of the RI in these vessels was not possible.

The authors of this chapter have now conducted a transvaginal ultrasound study of uterine blood flow with the NASG in 18 non-pregnant, normal, healthy female volunteers of reproductive age. Using Doppler ultrasound to identify both the internal iliac artery and the uterine artery, RIs were calculated as an approximation of uterine blood flow before, during and after placement of the NASG. The preliminary results demonstrate an increase in the RIs of both vessels. The RI of the uterine artery increased an average of 0.33 (SD 0.15, $n = 18$) from a mean of 0.72 (SD 0.094, $n = 18$) to 1.04 (SD 0.15, $n = 18$). Similarly, in the internal iliac artery, the RI increased 0.13 (SD 0.09, $n = 18$) from 0.91 (SD 0.06, $n = 18$) to 1.04 (SD 0.16, $n = 17$). These studies are ongoing. In addition to recruiting more volunteers, future studies will focus on postpartum patients and better delineating the pelvic blood flow in parturient patients.

Intra-abdominal pressure

The sole manufacturer of the NASG is Zoex (Coloma, CA, USA). The manufacturer's brochure states that the pressure exerted by the NASG is between 20 and 40 mmHg; however, published studies of the impact of the NASG on intra-abdominal pressure, whether in male or female volunteers, are not available⁵⁴.

In the absence of such information, the authors conducted preliminary investigations of the intra-abdominal pressure generated by NASG placement on 20 healthy female volunteers of reproductive age. Standard urodynamic equipment and minimally invasive techniques routinely performed in clinical gynecologic evaluations were employed. A 2.3 mm rectal pressure catheter (7 Fr, aircharged™ abdominal catheter; T-DOC® Company, Wilmington DE) placed transrectally was used to approximate intra-abdominal pressure. Measurements were performed using the Triton urodynamic monitor (Laborie Medical Technologies, Inc, Williston, VA) attached to the rectal pressure catheter. This technique provided a minimally invasive, accurate approximation of intra-abdominal pressure and allowed measurements to be taken continuously throughout the study. Preliminary results demonstrated a mean increase of 15.3 mmHg (SD 5.60).

DISCUSSION AND CLINICAL IMPLICATIONS

The evidence presented in this chapter supports the theoretical model of NASG function. Compression of capacitance vessels in the lower extremities appears to

produce a shifting of pooled blood back into the central circulation. The rapid recovery of the shock index and vital sign recovery times reported in clinical trials to date suggest that this may occur. An evaluation of the impact of the NASG on cardiac output and central venous return is needed.

In the pelvic vasculature, the distal aorta branches into the common iliac artery which in turn branches into the external iliac which proceeds to become the femoral in the leg and the internal iliac artery, which supplies the majority of blood flow to the uterus via the uterine arteries. Three studies have now evaluated lower abdominal and pelvic blood flow with NASG placement; all demonstrated decreased flow in the distal aorta and increased resistive indices in the internal iliac and uterine arteries. These findings are consistent with the decrease in blood loss from PPH that has been reported in published studies of the NASG²⁶⁻²⁸. The observed increase in the RI of the internal iliac and uterine arteries with NASG application provides a physiologically plausible mechanism to explain how hemorrhage is reduced by NASG application.

Both NASG efficacy and potential side-effects (oliguria and/or dyspnea) probably depend on the circumferential compression of vessels from pressure exerted by the device; therefore, understanding how pressure varies in individual applications is of critical importance. The studies cited above demonstrate that both internal and external abdominal pressure increase with NASG application, and that the pressure generated likely varies with applicator strength and patient BMI. The NASG has no pressure gauge or mechanism to inform applicators that the appropriate pressure is being exerted. This initial evaluation of pressure variation among patients and applicators provides critically important baseline information that can inform development of means to ensure that appropriate pressure is exerted with each application of the NASG.

Severe PPH affects a diverse cohort of over 100,000 women annually throughout the world^{2,55}. In pre-intervention phase/NASG-intervention phase studies in tertiary facilities, use of the NASG enhanced maternal outcomes for women, including a significantly reduced blood loss. The initial blood flow studies seem to indicate that NASG application increases RI and helps explain how the NASG decreases blood loss. Although the science behind the success of the NASG has advanced compared to the available knowledge even a decade ago, much remains to be learned about this device. The available pressure studies indicate that body size and strength of the person applying the garment are important.

The garment could affect outcomes. Because the body habitus of a woman affected by PPH in rural India may be very different than a woman in peri-urban Nigeria or in the Peruvian highlands, it is important to consider height, weight, BMI and habitus of prospective patients. Similarly, health care providers vary in size and strength; the maximal pressure generated by a taller, stronger applicator is likely to be significantly different than a smaller, shorter,

weaker applicator. It may be that individualized training methods could be developed to better standardize the amount of pressure generated. Alternatively, it may be beneficial to develop a simple pressure gauge, or other means of ensuring appropriate garment placement in patients with different body habitus.

FUTURE DIRECTIONS

The ideal amount of pressure that should be generated with NASG application is not known. Moreover, the current sole manufacturer of the device provides no information regarding the necessity or lack thereof to apply more or less pressure dependent on the size of the patient. Studies to more fully elucidate the impact of the NASG on intra-abdominal vascular flow would clarify the relationship between pressure applied and perfusion of intra-abdominal organs (e.g. uterus, intestines, kidney). It would also be important to correlate the pressure exerted by the NASG with the cardiovascular impact on the central circulation, namely central venous pressure, systemic vascular resistance and cardiac output.

Future studies should expand the sample size and recruit a larger number of participants with different body habitus, including height, weight, BMI, abdominal circumference and ethnicity. It may also be useful to conduct this study in a postpartum cohort, as the physiology of pregnancy and the puerperium may result in some important differences in pressure outcomes. Similarly, the effect of applicator size and strength should be further explored by evaluating a more diverse cohort of applicators with varied height, weight, strength, gender and ethnicity, and using a standardized method of strength testing to evaluate applicator strength and its correlation to pressure. It is also likely that differences in effect exist based on the intra-vascular volume status of the patients. The effect of the NASG on cardiac output may be greater or different in a severely hypovolemic patients. It would be useful to conduct studies in patients who have experienced PPH and shock to evaluate the cardiovascular impact of the NASG in this cohort.

Understanding how pressure, vascular flow and cardiovascular function are related in a diverse cohort of patients and health care providers is an important step towards optimizing NASG application. Future studies should endeavor to define this relationship and to more clearly elucidate the individual characteristics that affect NASG application. If significant variation persists in future studies, modification of NASG design (e.g. simple pressure gauge) or improved training protocols may result in improved individual application.

The goal of these future studies would be to ensure that each placement of the NASG will result in optimal results: immediate diminished uterine bleeding, resuscitation from shock, and survival without adverse effects. Achieving this objective may improve obstetric shock management and reduce deaths from obstetric hemorrhage, the world's leading cause of maternal mortality.

PRACTICE POINTS

- The NASG reduces the time to recovery from shock as demonstrated by improvement in vital signs and the shock index, as well as improved survival
- The NASG decreases blood loss by increasing the resistive index in the internal iliac and uterine arteries, which indicates decreased blood flow through these vessels
- The NASG increases both external and internal abdominal pressure; preliminary data suggest that the amount of increase in intra-abdominal pressure is 10–20 mmHg
- There may be variability in effectiveness of the NASG depending on individual patient characteristics such as BMI and abdominal circumference. This area warrants additional research.

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