MODELING THE EFFECTS OF INTRA-ABDOMINAL HYPERTENSION

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ABSTRACT
Intra-abdominal hypertension denotes elevated pressure in the abdomen. Such hypertension is common in patients in critical care hospital wards. The consequences of intra-abdominal hypertension involve constrained blood flow to vital organs such as the kidneys and abdominal organs (in connection with reduced cardiac output) potentially leading to multi-organ failure) Intra-abdominal hypertension represents an independent risk factor for mortality in acute and intensive care patients. Even given these observations, this condition is not always adequately monitored and much remains to be learned about its evolution and its impact on cardiovascular function. In addition, no significant modeling studies or models have been proposed to study this phenomenon. In this paper, we will discuss this problem, relevant mechanisms, and a model to simulate the effects of intra-abdominal hypertension on the cardiovascular system.

Keywords: venous return, systemic resistance, blood flow, Abdominal Compartment Syndrome, renal failure

1. INTRODUCTION

Intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) (Ivaturi et al [2006], Li [2012]) have only recently received significant attention. In fact, the World Society of the Abdominal Compartment Syndrome which defines the four grades of IAH was only established in 2004. The establishment of this society was in recognition of the importance, prevalence, and negative consequences of IAH in critically ill hospital patients. IAH is recognized as an independent risk factor for death in intensive care patients.

Definitions

Intra-abdominal pressure (IAP) is the pressure within the abdominal cavity. Typical steady state values for IAP in normal healthy individuals are 0 to 5 mm Hg. IAH is diagnosed if the IAH is greater than 12 mmHg either over a continuous period or with repeated episodes. IAH is divided into four grades with grade IV IAH reflecting pressure greater than 25 mmHg.

Consequences

The abdomen includes many important organs including the intestines, kidney, and liver. IAH can influence the function of such systems (De Waele and De Lit [2007] and in particular cause a local reduction in blood perfusion to such organs leading to organ damage (see, e.g., Shibagaki [2006]). In addition, IAH can reduce venous return thereby affecting organ systems outside of the abdominal region such as interfering with diastolic filling of the heart and thereby reducing cardiac output. These effects can in turn influence blood perfusion in the brain.

2. MOTIVATION AND METHOD

Limited modeling studies exist related to intracellular and extracellular fluid volume change which may influence IAP (Tartara and Tashiro [2007]) and little modeling on the influence of IAP on hemodynamics. We describe a mathematical model that can in a straight forward way be adapted to test the impact of increased abdominal hypertension. The ultimate goal is to develop a test model of IAH which will provide the basis for a more comprehensive model that can provide qualitative analysis of the consequences of IAH and potentially lead to important insights for detection of IAH in the clinical critical care setting. Given the number of cardiovascular consequences of IAH, such a model for diagnosis or diagnostic training would be very useful.

3. MODEL

The mathematical model is adapted from a model for examining orthostatic stress using experiments from lower body negative pressure (LBNP) and head up tilt or (HUT) and blood loss due to hemorrhage (Batzel et al [2006, 2009], Kappel et al [2007], Fink et al [2004]). Based on the above applications, the model is very well suited for the proposed extension to study IAH. In particular:

1. The initial model includes 10 compartments (Figure 1) representing various body tissues compartments as well as control mechanisms, and plasma-interstitial fluid exchange. The model thus distinguishes between the abdominal compartments and other compartments.
2. The implementation of changes in transmural pressure in intra-abdominal vessels can be directly applied via the application of positive intra-abdominal pressure on the vasculature.
3. The model focuses on control responses which will also be a focus here. Unstressed venous volume also is implemented in the model which is relevant for the current proposed work.

Mass balance relations

Model compartment equations are mass balance relations. The generic form for these mass balance relations is illustrated in the equation below where for a generic compartment comp in Figure 1, *P* represents the pressure, *c* compliance, *V* the volume of the compartment, *F* the flow (in and out) of a compartment, and V_u unstressed volume:

$$(1)\quad c\frac{dP_{comp}}{dt} = F_{in} - F_{out} - \frac{dc}{dt}\left(P_{comp} + P_{bias}\right) - c\frac{dP_{bias}}{dt} - \frac{dV_u}{dt}$$

Transmural pressure can be implemented via positive or negative changes in the term P_{bias}.

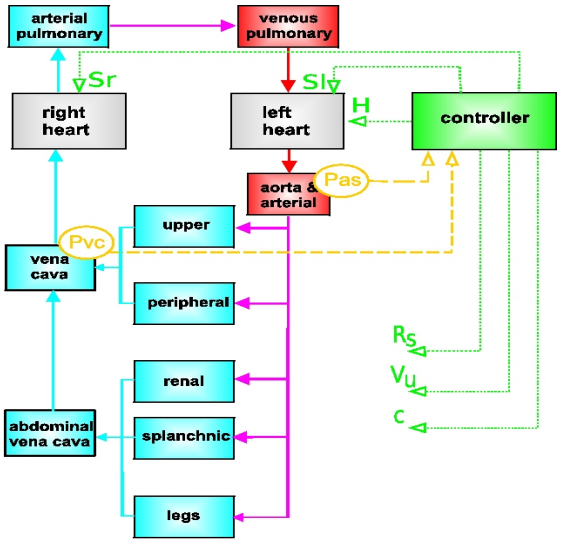

Figure 1: Model block diagram

The model incorporates lumped volume compartments where each compartment is considered to be a vascular compartment of blood or fluid characterized by the total fluid volume, by fluid pressure, and by vascular compliance (that reflects the vascular stretch due to pressure). Compartmental unstressed volume V_u represents the volume of a compartment before the vascular walls are subjected to a transmural pressure that stretches the vascular wall to accommodate the incorporation of additional fluid volume. The control of unstressed volume is an important response to loss of dynamic blood volume (the volume under pressure).

Flows between compartments

The equation for blood flow in or out of a compartment takes the form of Ohm's law so that, for example, the left equation below describes the flow into the upper body compartment dependent on arterial and venous pressures depicted in Figure 1 and the right equation give the flow into the splanchnic region:

$$(2)\qquad F_{up,in} = \frac{P_{as} - P_{vc}}{R_{up}} \text{ and } F_{spl,in} = \frac{P_{as} - P_{avc}}{R_{spl}}.$$

An important mechanism to consider is the impact of IAH on vascular resistances due to constriction of vessels under positive transmural pressure (see below). Additional features included in the vascular flow structure includes venous valves to block back flow and also minimal flow constraints that act as autoregulatory action to override the baroreflex control of vascular resistance which induces contraction in certain arterioles to support blood pressure.

Cardiac output

Cardiac output is determined by heart rate and stroke volume. The latter is determined by ventricular preload and afterload and a relation for heart muscle contractility determined by state equations for contractility influenced by heart rate (see Batzel et al [2009]). The model is nonpulsatile as currently configured but pulsatile effects can be implemented as in Olufsen et al [2005].

Control mechanisms

The model incorporates control response to changes in arterial pressure P_{as} and venous pressure P_{vc} through the baroreflex which alters heart rate *H*, (and hence indirectly heart muscle contractility *S*), unstressed volume V_u, compliance *c*, and vascular resistance *R* (See Figure 1 controller) to stabilize arterial pressure after perturbation from a steady state operating point. These controls are based on the model of Olufsen et al [2005].

1. Each control equation is described in terms of a set point function and a differential equation that determines the dynamics of the control response based on deviations in the arterial and venous blood pressures

2. Arterial pressure is sensed by the arterial baroreceptors in the aorta and carotid bodies and venous pressure by the cardiopulmonary sensors in and around the right atrium and in the pulmonary circuit
3. Mobilizable unstressed volume which can be shifted to dynamic circulation to support blood pressure is incorporated into several compartments including the lower body (legs) compartment and in the splanchnic region (abdomen, intestines, and including liver) and kidneys. In addition the global control of systemic resistance is apportioned proportionally to the arterial vascular elements subject to a maximal increase that ensures a minimal blood flow (autoregulatiory effect).

Fluid volume control and exchange with interstitium
The exchange of fluid between the interstitial space and the vascular space is an important mechanism for regulating volume in normal healthy individuals and also in patients depending on dialysis {Schneditz [1992, 2005]). The current model includes a submodel of this exchange which can aid in supporting circulating blood volume. This aspect of fluid volume control can have important effects on interstitial volume and edema which can have negative effects on structures such in the microvasculature.

Additional model details for the model given in Figure 1 can be found in Appendix A.1 of Batzel et al [2009].

Model adaptations for IAH and validation
Model adaptations to reflect IAH need to include several effects produced by a relative increase in exterior pressure relative to the internal pressure of key organs (compartments) and the vascular structures (arteries and veins) connecting them. This pressure differential will be referred to as a positive transmural pressure (exterior to interior). In contrast, during studies using lower body negative pressure (LBNP), exterior air pressure is reduced creating a negative transmural pressure differential that stretches the vascular elements causing pooling of blood in compartments where the negative pressure is applied. This acts as an effective sequestration of blood reducing the blood volume under dynamic pressure which determines blood flow.

The key effects to consider include the following.

1. IAH influences the transmural pressure and this effect will be introduced via a positive bias pressure P_{bias} in the mass balance equation of form (1) for any compartment subject to IAH. This pressure acts to reduce the compartment volume. A positive bias pressure will be applied to the abdominal compartments (abdominal vena cava, renal, and splanchnic compartments).

2. This positive pressure will also reduce compartment volumes of inflow arteries and arterioles (incorporating capillaries) and outflow venules and veins, changing the vascular flow resistances. Such variations in inflow and outflow resistances reflect constriction due to the positive external pressure applied to arteries and veins. This effect can be implemented as variations in inflow and outflow resistance parameters but the effects are complex and a comprehensive model will require additional modeling studies to implement.

The changing hemodynamic environment due to pressure changes and resistances can influence blood flow to organs where IAH exists and may also cause changes in cardiac output and cerebral blood flow. These interactive effects are under investigation in current work.

The model can be used to assess in particular the interaction of several key variables including

- Changes in intra-abdominal pressure
- Changes in vascular resistances to abdominal blood inflow and outflow
- Degree of lower body blood volume sequestration
- Venous return
- Arterial and femoral, blood pressure and intracranial pressure.

4. FIRST SIMULATIONS

The following figures are generated with a +10 P_{bias} induced at t=0 over a period of 1 minute and applied to the abdominal vena cava, splanchnic, and renal compartments. No change in arterial resistance is assumed for these simulations. Pressures are provided in Figure 2 and control responses in Figure 3.

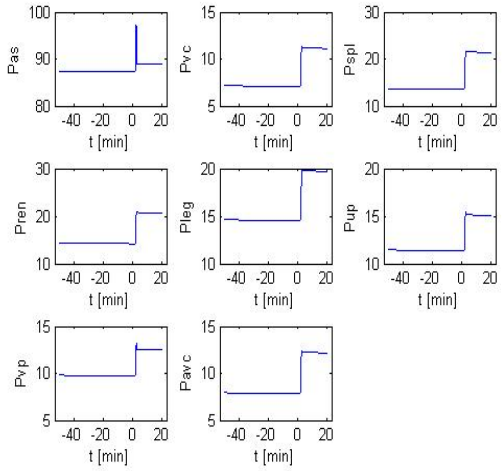

Figure 2: Model outputs for pressures. P represents pressure, for the various compartments in Figure 1.

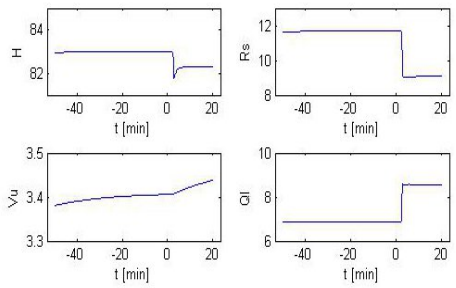

Figure 3: Model outputs for controls and cardiac output, V_u represents unstressed volume control. H represents heart rate, while Rs represents systemic resistance, and Ql left ventricular cardiac output,

Figure 2 and Figure 3 illustrate the impact of a change in $P_{bias..}$ pressure alone. The following points are made:

1. In general the compartment pressures rise as a consequence. of the external pressure which physiologically act to compress compartment volumes. In terms of modeling the bias pressures reduces the volume via the difference between pressure P *and* P_{bias} in (1).
2. The increase in pressures generate and perhaps are partly produced by an increase in left cardiac output $Q_{l.}$ as depicted in Figure 3.
3. As a consequence of the spike in P_{as} shown in Figure 2, the control response acts to reduce systemic resistance R_s in Figure 3 which also acts to increase $Q_{l.}$.

The above effects are due only to the change in $P_{bias..}$ Additional factors must be included to reflect various effects of IAH. As mentioned above, it certainly is the case that IAH constricts arteries and veins. Currently in the model, no direct impact of IAH on resistances is included.

Arterial and venous blood flow resistances R are currently incorporated in the model as resistance to flow between compartments as given in (2). An increase in local resistance due to constriction induced by IAH can be implemented as a local increase in resistance in those vascular elements subject to IAH. This will impact, in conjunction with other effects such as pressure differentials between compartments, the blood flow to those compartments. In turn, reduced blood flow could damage tissues such as is sometimes seen in the kidneys of patients with IAH. In fact high compartment pressures may also have an impact as discussed below.

In the above simulations, cardiac output rises due to the global control response of reducing resistance (Figure 3) in response to the spike in arterial pressure (Figure 2). Including an additional effect of increasing local resistance due to constriction caused by IAH will counteract this effect and will certainly increase flow resistance to compartments where IAH is experienced. The net result could reduce overall cardiac output.

5. DISCUSSION

An important area where IAH has serious consequences is in kidney function (Mohmand and Goldfarb [2011]), Renal dysfunction is a common early consequence of IAH with renal hypoperfusion beginning approximately at abdominal pressures of 8-12 mm Hg and peritoneal dialysis is a risk factor for IAH (Shibagaki et al [2006]). The mechanisms by which IAH can influence renal health and function include many factors including reduced cardiac output, increased renal vascular resistance, and decreased glomerular filtration etc.

In addition the increase in compartmental renal pressure can have a negative impact on renal tissue health and function, which could reflect intrarenal venous congestion and also act to reduce the renal filtration rate seen in renal function under IAH .(Mohmand and Goldfarb [2011]).

The overall impact of IAH can extend beyond those compartments where IAH is induced. Figure 2 indicates that just the inclusion of positive bias pressure in some compartments can cause pressure changes even in compartments where IAH is not induced. In addition other effects can be introduced. For example, intracranial pressure has been observed to rise Mohmand and Goldfarb [2011]),

Recently the problem of IAH has been given greater attention in critical care situations where IAH can arise as a consequence of several factors including techniques during surgery. Increased efforts have been made to monitor and probe for IAH in critical care patients and greater efforts have also been made to train critical care workers in this area. A well validated model of IAH could be used to aid in this training and in testing the hemodynamic implications of IAH.

SUMMARY

As can be seen from the above discussion, the interaction of local effects of IAH and global control response to perturbations in steady state pressures and flows is very complex. Quantifying these interactions can lead to better detection and treatment in patients as well as better training for those dealing with IAH, especially in the critical care area. Further work will be directed to generate a more comprehensive model of the effects and interactions of mechanisms related to IAH.

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