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COMPUTATIONAL ANALYSIS OF RENAL ARTERY FLOW CHARACTERISTICS BY MODELING AORTOPLASTY AND AORTIC BYPASS INTERVENTIONS FOR ABDOMINAL AORTIC COARCTATION

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ARTICLE HIGHLIGHTS

Type of Research: 1. Single-center retrospective case study

Key Findings: Supra-renal abdominal aortic coarctation (SAAC) was associated with high frequency disturbances in the renal arteries that could trigger increased renin release in the kidneys, leading to secondary hypertension. In general, surgical repair reduced but not eliminated these disturbances.

Take home Message: High frequency disturbances in the renal arteries could explain the limited hypertension success rates of surgical repair for SAAC. Patient-specific computational modeling offers a valuable tool to analyze complex hemodynamics in vascular disease and test the hemodynamic performance of different surgical interventions.

Table of Contents Summary

This retrospective case study used analyzed aortorenal hemodynamics in a patient with a SAAC and found that SAAC is associated with high frequency disturbances in the renal arteries that could trigger renin release, resulting in secondary hypertension. Surgical repair with TAB or PA reduces aortic pressures, but does not always eliminate the high frequency disturbances, explaining the limited hypertension success rates of these procedures.

ABSTRACT

Objectives: Suprarenal abdominal aortic coarctation (SAAC) alters flow and pressure patterns to the kidneys and is often associated with severe angiotensin-mediated hypertension, refractory to drug therapy. SAAC is most often treated by a thoracoabdominal bypass (TAB) or patch aortoplasty (PA). It is currently unclear what effect these interventions have on renal flow and pressure waveforms. This study, using retrospective data from a SAAC patient subject to a TAB, undertook computational modeling to analyze aortorenal blood flow preoperatively as well as postoperatively following a variety of TAB and PA interventions.

Methods: Patient-specific anatomical models were constructed from preoperative computed tomographic angiograms of a 9-year old child with an isolated SAAC. Fluid-structure interaction (FSI) simulations of hemodynamics were performed to analyze preoperative renal flow and pressure waveforms. A parametric study was then performed to examine the hemodynamic impact of different bypass diameters and patch oversizing.

Results: Preoperative FSI results documented diastolic-dominated renal perfusion with considerable high frequency disturbances in blood flow and pressure. The postoperative TAB right and left kidney volumes increased by 58% and 79%, respectively, reflecting the increased renal artery blood flows calculated by the FSI analysis. Postoperative increases in systolic flow accompanied decreases in high frequency disturbances, aortic pressure and collateral flow following all surgical interventions. In general, lesser degrees of high frequency disturbances followed PA interventions. High frequency disturbances were eliminated with the 0% PA, in contrast to the 30% and 50% PA oversizing and TAB interventions in which these flow disturbances remained.

Conclusions: Both TAB and PA dramatically improved renal artery flow and pressure waveforms, although disturbed renal waveforms remained in many of the surgical scenarios. Importantly, only the 0% PA oversizing scenario eliminated all high frequency disturbances, resulting in near normal aortorenal blood flow. The study also establishes the relevance of patient-specific computational modeling when planning interventions for the midaortic syndrome.

Clinical Relevance.

We performed computational fluid dynamics (CFD) modeling to assess aortorenal blood flow in a child with a supra-renal abdominal aortic coarctation (SAAC) and test the performance of different surgical interventions. We discovered high-frequency disturbances in the renal arteries that could potentially triggering excessive renin release. Thoracoabdominal bypass and patch aortoplasty with oversizing did not remove these disturbances completely. This could explain why the hypertension cure rates of surgical repair of SAAC are suboptimal. Additionally, this study establishes the relevance of CFD modeling as a valuable tool to analyze complex hemodynamics and test the performance different surgical interventions.

INTRODUCTION

Suprarenal abdominal aortic coarctations (SAAC) are often associated with renal arterial stenoses and severe renin-mediated arterial hypertension.[1] In these circumstances, the increased blood pressure and development of collateral vessels circumventing the aortic and renal artery narrowings tend to increase mean renal blood flow toward normal. However, this response is inadequate and the abnormal release of renin persists. Whether the principal cause of the abnormal renin release is due to decreased renal artery pressure or abnormal renal artery flow waveforms is an unsettled issue.

The abnormal renin release and angiotensin generation coupled with secondary increases in aldosterone production make this form of hypertension refractory to most drug therapies. Lowering the systemic arterial pressure with drugs without treating the aortic and renal artery narrowings only results in further diminutions of intrarenal blood flow and continued excesses in renin production. Because of these medical failures, restoration of normal renal blood flow by open operative or endovascular interventions have evolved as the favored means of managing this disease.

The University of Michigan’s history of treating occlusive lesions of the renal arteries and abdominal aorta in pediatric patients has extended for more than 4 decades.[1–6] Postoperative blood pressure control in this experience has been optimal when treating patients with isolated renal artery stenoses, in contrast to less salutary outcomes when the renal artery procedures have been accompanied by a thoracoabdominal bypass (TAB) or patch aortoplasty (PA) for a coexisting abdominal aortic coarctation. Even after successful anatomic aortic and renal artery reconstructions, postoperative hypertension has been noted to persist.[1,7,8]

It is hypothesized that the aortic reconstructive procedures may not normalize renal artery blood flow. A TAB from above a SAAC to below the renal arteries may cause turbulent and abnormal renal artery perfusion as retrograde aortic flow encounters antegrade flow in the region of the renal vasculature. In addition, performance of a PA, given the commonplace practice of oversizing the patch in younger patients to accommodate for later growth, may also result in abnormal renal blood flow and contribute to the persistence of the hypertensive state.

METHODS

Aortorenal blood flow was retrospectively studied using patient-specific fluid-structure interaction (FSI) simulations in a child that was treated for a SAAC. Subsequently, the impact of the most commonly undertaken surgical repairs (TAB and PA) on aortorenal blood flow was analyzed. The study was approved by the University of Michigan Board of Review (HUM00112350 and HUM00006223).

Patient history. A 9-year-old girl was referred to the authors' institution with a diagnosis of middle aortic syndrome and renin mediated hypertension. Her initial elevated blood pressures in the 130-150/90-95 mmHg range were only modestly improved to the 140/80 mmHg range following treatment with a beta-blocker and calcium channel blocker. In addition, she initially complained of lower extremity weakness and fatigue that was progressive with activity. Duplex Doppler ultrasonography estimated a pressure gradient of 58 mmHg across the SAAC. She was considered an appropriate candidate for surgical repair of the abdominal aortic coarctation.

Imaging data. Preoperative anatomy and hemodynamic data were obtained using duplex Doppler ultrasonography, computed tomography angiography (CTA) and phase contrast magnetic resonance imaging (PC-MRI). CTA imaging revealed a SAAC of 15 mm in length, with a 2.5 mm anterior-posterior diameter, and no renal artery involvement (Figure 1). The celiac artery (CA) and superior mesenteric artery (SMA) arose from the coarctation itself, and both exhibited ostial narrowings. Extensive collaterals circumvented the coarcted aorta, with an intact inferior mesenteric artery (IMA) being the dominant source of blood flow to the intestines. The internal mammary arteries were enlarged and communicated with the epigastric arteries that had multiple collaterals to the lower extremities and abdominal visceral organs. MRI examinations performed at 10-day and 1-year after the TAB provided postoperative data for analysis.

Thoracoabdominal bypass. The basis for choosing a TAB over a PA was that the 2.5 mm diameter of the coarctation and the involvement of the CA and SMA would have made an aortoplasty inordinately challenging and risky. In this case a midline abdominal incision was made from the xiphoid to the pubis, followed by medial visceral rotation of the left colon, to provide exposure of the entire abdominal aorta.

The supra celiac aorta was occluded with a Satinsky clamp, following which a 14 mm polytetrafluoroethylene (PTFE) bypass graft was anastomosed to a lateral aortotomy. The proximal aorta was occluded for 17 minutes during which time blood flow to the lower extremities and abdominal viscera, although reduced, was maintained through the preexisting large retroperitoneal and abdominal wall collaterals. The graft was then clamped just beyond its aortic origin and antegrade aortic blood flow was restored following removal of the supraceliac aortic clamp. The graft was passed behind the left kidney and then anastomosed in an end-to-side manner to a lateral aortotomy just above the IMA (Figure 1). During the distal anastomosis, the infrarenal aorta was occluded for a time similar to that of the proximal anastomosis.

~~***Thoracoabdominal bypass***. The basis for choosing a TAB over a PA was that the small diameter of the coarctation and the involvement of the CA and SMA would have made an~~

~~aortoplasty inordinately challenging and risky. A 14 mm polytetrafluoroethylene (PTFE) bypass graft originating from the supra-celiac aorta was carried to the infra-renal aorta proximal to the IMA (Figure 1). The procedure was performed without complications and the patient was discharged with resolution of her lower extremity discomfort. However, she remained mildly hypertensive postoperative and at 1-year follow-up; she remained on a low dose calcium channel blocker with resting blood pressures in the 110-115/65-70 mmHg range.~~

Kidney Size. ~~Analyzing the preoperative and 10-day follow-up imaging data, an increase in kidney length was observed. Following this finding, p~~Preoperative and 10-day postoperative kidney volumes were measured using semi-automatic segmentation tools in Mimics version 21.0 (Materialise NV, Leuven, Belgium).

Computational modeling. Patient-specific FSI simulations[9] were performed to assess preoperative blood flow and compare the hemodynamic performance of TAB versus PA using a "virtual testing" paradigm ~~(Figure 2)~~.[10] First, a preoperative model was created and calibrated to match the anatomical and hemodynamic clinical data (Figure 2~~3~~). Then, the calibrated preoperative model was adapted to reflect six surgical interventions (Figure 3~~4~~), including three different TABs with 12 mm, 14 mm and 16 mm diameters, respectively (TAB-12mm, TAB-14mm and TAB-16mm); and three different PAs producing increases in aortic diameters of 0%, 30% and 50% (PA-0%, PA-30% and PA-50%) relative to the native aorta. Additionally, a control case was constructed by adjusting the preoperative model to produce a healthy anatomy without coarctation and collateral vessels (Appendix Figure 3).

~~The preoperative and six surgical repair~~ All models were constructed from the CTA image data using ~~the cardiovascular~~ CRIMSON (CardiovasculaR Integrated ~~modeling~~ Modeling and ~~simulation~~ SimulatiON) ~~software~~ version 2017.07.01, developed by King's College London

(London, UK) and the University of Michigan (Ann Arbor, MI) under the support of the European Research Council~~CRIMSON~~.[11] Besides the vascular anatomy, each FSI model requires specification of arterial wall material properties (thickness and stiffness) as well as outflow boundary conditions at each branch. These boundary conditions represent the compliance and resistance of the distal vasculature not included in the anatomical model. The wall properties and outflow boundary conditions were calibrated to match the simulation results with the clinically acquired flow and pressure data and achieve reasonable~~physiologic~~ regional flow distributions~~[13]~~ (Figure 2~~3~~).[12] The methods for specification of the boundary conditions and material properties are reported in detail in the Appendix. In the control case, the boundary conditions were tuned to match the preoperative flow splits and a blood pressure appropriate for this patient's size and age (96/65 mmHg).[13] In the postoperative models, cardiac output and outflow boundary conditions were kept the same as preoperative; with the exception of the supra-aortic arteries, where the outflow boundary conditions were adjusted to reproduce literature data on regional flow splits.[14]~~maintain similar flow rates as preoperative. By doing so, the effects of cerebral autoregulation were taken into account.~~

Computations. -Blood was modeled as an incompressible Newtonian fluid with a density of 1,060 kg/m^3 and a dynamic viscosity of 4.0 Pa·s. Computations were performed using the CRIMSON Navier-Stokes flow solver on 160 cores at the University of Michigan high-performance computing cluster ConFlux. Simulations were run until cycle-to-cycle periodicity was achieved in the pressure fields, this typically took three to five cycles. Computation time per cardiac cycle was approximately 48 hours.

RESULTS

Postoperative course. Complete resolution of the patient's lower extremity discomfort was evident in the early postoperative period. Her serum creatinine which ranged from 0.48 to 0.57 mg/dL preoperatively, decreased to 0.28 to 0.3 mg/dL postoperatively. However, she remained mildly hypertensive during her postoperative hospitalization, and at 1-year follow-up she remained on a low dose calcium channel blocker with resting blood pressures in the 110-115/65-70 mmHg range.

Preoperative Simulation. The baseline preoperative model successfully reproduced the patient's hemodynamic data, as documented in a comparison between clinical data and simulation results at different locations in the circulation (Figure 2~~3~~). The computed flows were all within 5% of the clinically measured data, and computed pressures were within 10%.

The FSI simulation results revealed a pressure gradient of 55 mmHg across the coarctation at peak-systole (Figure 4~~5~~), which matched the pressure gradient derived from duplex Doppler ultrasonography (58 mmHg). Additionally, disturbed flow patterns were present distal to the coarctation which propagated into the renal arteries. Assessment of the renal artery flow and pressure waveforms revealed diastolic dominated renal flows with high frequency oscillations (Figure 4~~5~~ and Video 1). Renal artery pressure was markedly lower than ascending aortic pressure.

In the control case, systolic dominated renal flows without high-frequency disturbances were found. The results for the control anatomy are presented in Video 1 and Appendix Figure 3. A direct comparison of the pressure and flow waveforms between preoperative and control cases is reported in Figure 5.

Postoperative Simulations. The computed mean flows at the outlets of the preoperative model and all six surgical repair models (Table 1) were revealing. All six interventions successfully reduced pressures at the ascending aorta (Figure 6) and increased renal artery flow rates (Table 1). Furthermore, all surgical repairs resulted in systolic dominated flow waveforms (Figure 7), with a reduction of the high frequency flow and pressure disturbances in the renal arteries (Figures 7 and 8). Although most postoperative simulations retained some degree of the high frequency oscillations, the PA-0% eliminated the high frequency oscillations completely.

The flow waveforms from the TAB-14mm simulation were compared with the PC-MRI data at 1-year follow-up (Figure 9). The patient's cardiac output decreased during follow-up (-13%, from 3.9 to 3.2 L/min). The shape of the waveform changed as a result of a reduction in ventricular afterload following surgery. The computed (TAB-14mm) and 1-year follow-up PC-MRI data on flow through the bypass documented an excellent match: the percentages of cardiac output through the bypass were 38% and 39% for the computations and the PC-MRI data, respectively.

Kidney Size. Considerable changes in the kidney length ~~volumes~~ were noted at 10-day follow-up. To accurately quantify the change in kidney size, volumetric measurements of both kidneys were obtained (Figure 10~~9~~). Right and left kidney lengths increased from 3.4 to 3.85 cm (+13%) and from 3.8 to 4.6 cm (+21%), respectively. Right and left kidney volumes increased from 50.3 to 79.6 cm^3 (+58%) and 51.5 to 92.0 cm^3 (+79%), respectively. The observed increments in kidney volume reflected the calculated increases in right and left renal flow from the TAB-14mm FSI analysis (+9% and +26%, respectively).

DISCUSSION

Abdominal aortic coarctation is a rare vascular disease recognized most frequently in pediatric-age patients. The aortic narrowings are commonly associated with ostial stenoses of the celiac, superior mesenteric, and renal arteries.[15] This is clinically referred to as the middle aortic syndrome, which manifests in most patients with drug therapy resistant arterial hypertension.[16]

Classic canine experiments noted that the location of the abdominal coarctation plays a key role in the presence of hypertension.[17] Hypertension is commonly observed in cases where the coarctation is suprarenal or involves the renal arteries. Conversely, hypertension is mostly absent when the coarctation is distal to the renal arteries. An investigation by Scott et al.[18] of canine hypertension due surgically induced coarctation of the aorta that resulted in hypertension at 5 to 7 weeks, noted that transposition of a kidney to a level above the coarctation and contralateral nephrectomy resulted in disappearance of hypertension. These earlier experiments suggest that disturbed aortorenal blood flow contributes to hypertension in abdominal coarctation.

When treating middle aortic syndrome, conventional surgical reconstructive procedures and catheter-based interventions are favored over long-term drug therapy.[1,7,19–22] Operative planning is usually derived solely from preoperative imaging.[23] Surgical decisions are often based on technical issues at hand, rather than aiming to restore normal aortorenal blood flow. Unfortunately, endovascular balloon dilation with or without stenting of abdominal aortic narrowings has had limited use with mixed early results and few long-term successes. Open operations, such as TAB and PA, have been the most common form of treating abdominal aortic coarctations. These operations often lead to improved hypertension control, yet most cases still depend on antihypertensive therapy to maintain normal blood pressures for gender and age.

Many factors go into decision making for performing a PA versus a TAB. A PA is favored in most instances of a limited aortic coarctation distant from the CA, SMA and renal arteries. When assessing the long-term benefits of PA in younger patients, the patch is intentionally oversized to account for the child's expected growth. Nevertheless, the appropriate degree of patch oversizing has not been established. Likewise, the effects on renal artery blood flow accompanying a disproportionately enlarged aorta following a PA are unknown.

A TAB is the procedure of choice when treating more severe coarctations with abdominal aortic diameters of only a few millimeters. In this case, a PA would have near-overlapping sutures from the lateral walls of the patch. In the past, the authors have recommended a wide range of TAB diameters related to age, with the intent that the bypass diameter would at least be 60% to 70% of the predicted adult aorta.[1] These recommendations may be logical, but as noted with PA oversizing, the science behind such is meager.

Clinical Experience. Recently, the authors reviewed their experience with 155 children having renal artery stenotic disease and renovascular hypertension.[6] Hypertension outcomes were better in children treated with renal artery reconstructions alone compared to those requiring additional aortic procedures. The hypertension cure, improved, and failure rates in patients without aortic pathology (n=98) were 50%, 34% and 16%, respectively. These outcome rates were 33%, 59% and 8% in patients additionally treated with PA (n=28); and 35%, 50% and 15% in patients additionally treated with TAB (n=29). Given the poorer outcomes in patients undergoing concomitant aortic procedures, one must question whether abnormal aortorenal flow remains after surgery, and if differences exist between surgical repair with TAB and PA.

Computational Modeling. Computational modeling is a widely used method in engineering fields that can be applied to study complex flow dynamics. Image-based computational tools have been developed for cardiovascular disease research,[24,25] medical device evaluation[22] and, more recently, virtual planning of surgical interventions.[9] While in other engineering fields the ‘virtual testing’ paradigm has largely replaced the traditional ‘build-and-test’ (e.g. trial and error) paradigm, this is not yet the case in the medical field. As evident in the current investigation, the value of computational modeling is apparent in preoperative determination of the therapeutic impact of different sizes of TAB and PA in patients with the midaortic syndrome.

Computational modeling in this investigation provided data of much higher spatial (up to 0.05 mm) and temporal (0.025 ms) resolution than available in any contemporary imaging test. This high-resolution data revealed an unexpected and potentially relevant finding of high frequency disturbances in the renal arteries preoperatively that could explain an increased renin release in the kidneys, resulting in secondary hypertension. Persistent high frequency disturbances were also found in the postoperative models and might explain the continuing hypertension following both TAB and PA interventions in patients undergoing concomitant renal artery reconstructions.

Besides characterization of preoperative aortorenal blood flow, this study also analyzed the impact of different TAB diameters and degree of PA oversizing. In total, six different surgical treatment options were studied: three TAB diameters and three levels of PA oversizing. All surgical interventions resulted in reduced aortic pressures, and increased renal flows with restoration of systolic-dominated waveforms.

An unexpected finding of this investigation was that most surgical repairs resulted in a reduction in renal artery pressures (Figure 8). This acute response of the system, which does not account for any auto-regulatory processes following the surgery, is reflective of the large reductions in aortic pressures in all postoperative models (Figure 6).

Importantly, various degrees of high frequency disturbances persisted postoperatively, the exception being the treatment with a 0% PA which eliminated the high frequency disturbances completely. These results suggest that excessive PA oversizing and TAB lead to high frequency disturbances that may contribute to continued renin-mediated hypertension.

In the TAB operations, the high frequency disturbances could be explained by the turbulent mixing of antegrade flow through the remaining aortic stenosis and retrograde flow through the TAB. Changing the TAB graft diameter did not significantly impact the persistence of high frequency disturbances. Such flow abnormalities could explain why the patient in the present case report, who had undergone a TAB repair, was still dependent on anti-hypertensive medication at 1-year follow-up. In an oversized PA, the dilated segment of the reconstruction induces flow disturbances. Flow clearly shows complex recirculation and vortices in the region of the patch (Figure 11), similar to what is observed in aneurysmal disease. The absence of dilation in the PA-0% case explains the lack of disturbances in this model. Furthermore, it may also explain the reduced hypertension cure rates of renal artery revascularizations in the authors' larger series of patients requiring concomitant aortic procedures.

Historically, renin-mediated hypertension has been linked to low perfusion pressure and low renal blood flow.[23] The high frequency flow oscillations observed in the present work have not been described in the earlier literature. The most likely explanation for this is that contemporary clinical measurement devices lack the temporal resolution necessary to detect such high frequency flow oscillations. It has been recognized that Doppler ultrasonography, CTA and MRI can all be helpful in the evaluation of renovascular disease, but none have, at present, high enough sensitivity to rule out renovascular disease in a child with a suggestion of that diagnosis.[27]

Limitations. The stiffness properties of the aortic wall could not be calculated with the available data in this study. Therefore, in the present investigation, the assigned stiffness parameters were derived from a previous study from our laboratory which characterized aortic stiffness in a cohort of pediatric patients with aortic coarctation.[28] In that study, the aortic stiffness was calculated using strain measurements from MRI and invasive pressure measurements from catheterization.

This investigation analyzed aortorenal blood flow in a single patient with a suprarenal abdominal aortic coarctation. While the results for this patient were clinically-validated, performing the same analysis in patients with different anatomical features might result in different outcomes, including the presence of high-frequency disturbances in the renal arteries. Additionally, the causality between the high frequency disturbances and excessive renin release should be further investigated. Furthermore, we tested six different surgical interventions with arbitrary TAB and PA sizes. Performing a parametric study of other patch and bypass sizes and configurations could result in different outcomes~~.~~

Furthermore, it is important to note that even though a specific intervention might theoretically render a better hemodynamic outcome, performance of the procedure itself may be inordinately challenging and risky, resulting in a technical failure and less successful outcome. Thus, acceptance of benefits defined by virtual testing must be tempered by clinical judgement and expertise.

Lastly, the results presented here do not take into account any of the vascular auto-regulations that undoubtedly occur after a vascular reconstruction. The magnitude of the waveforms, specifically the pressure, might change as a result of systemic vasoreactivity, although the high frequency disturbances are likely to persist.

CONCLUSIONS

This study has revealed the presence of high frequency disturbances in renal blood flow and pressure following operative interventions for SAAC. These previously unrecognized disturbances may be a fundamental contributor to continued abnormal release of renin, and thus the basis of the often-seen persistent post-operative hypertension in this patient population.

Considerable value resides in computational modeling of vascular surgery procedures. Patient-specific modeling provides high-resolution hemodynamic information for differing interventions, and allows preoperative planning for complex procedures, such as those accompanying aortic reconstructions in young patients with SAAC. Collaborative efforts between biomedical engineers and clinicians will be essential to providing accurate modeling and simulation of feasible surgical procedures in this setting.

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