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Major vascular injury during gynecologic cancer surgery

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ARTICLE INFO	A B S T R A C T
Keywords Vascular injury Venous injury Arterial injury Gynecologic Surgery Intraoperative injury Vascular repair	Objective: Vascular injury during major gynecologic cancer surgery is a rare but potentially fatal complication. The purpose of this study was to review our experience with major vascular injury during gynecologic cancer surgery.Methods: This was a retrospective chart review of women undergoing surgery by our gynecologic oncology department from 7/1/99 to 6/30/20 who had a major vascular injury. We identified women who sustained a vascular injury by a combination of CPT code and medical record searches, fellow case logs and a list maintained for an ongoing quality assurance program. Data were expressed as median and range for continuous variables and as frequency and percentage for categorical variables. Fisher's exact test was used to analyze differences in complication rates between groups.Results: Major vascular injury was identified in 52 patients and procedures. The inferior vena cava was the most common site of injury, 32.7% (17/52), followed by the external iliac vein, 23.1% (12/52). Lymph node dissection was the most common time for a vascular injury to occur 51.9% (27/52). The majority of injuries required suture repair, 80.8% (42/52). Estimated blood loss in cases with vascular injury ranged from 100 mL to massive unquantifiable blood loss in the case of an aortic injury. Patients required a median of 2units of packed red blood cells. Postoperative complications included anemia requiring blood transfusion, 19.6% (9/46) and venous thromboembolism, 19.6% (9/46). Conclusions: Vascular injury remains a rare but potentially morbid complication of gynecologic oncologic sur- gery. Prompt recognition and management are imperative in minimizing persistent bleeding and complications.

1. Background

Vascular injury during major gynecologic cancer surgery is a rare but potentially fatal complication. The incidence of vascular injury during gynecologic surgery is reported to be 0.3–1.0%. (Nordestgaard et al., 1995; Sandadi et al., 2010; Haygood et al., 2014; Jones et al., 2014; Köhler et al., 2004; Querleu et al., 2006) The most commonly injured vessels during gynecologic surgery include the aorta, inferior vena cava, common, external and internal iliac arteries and veins as well as gonadal and mesenteric vessels. (Sandadi et al., 2010) Vascular injury can occur during both open and laparoscopic procedures during sharp dissection or electrosurgery and may additionally occur as a result of laparoscopic entry, regardless of technique. (Nordestgaard et al., 1995; Köhler et al., 2004; Nezhat et al., 1997; Agresta et al., 2004; Ahmad et al., 2007)

Various risk factors for vascular injury during abdominal surgery have been suggested, including obesity, adhesions, vascular aberrations and surgery at low volume surgical centers. (Salman et al., 2010; Herrmann and Wilde, 2016; Gyimadu et al., 2012; Sinno et al., 2017) Additionally, certain procedures commonly performed in gynecologic cancer surgery, such as lymphadenectomy, pose a higher risk for vascular injury due to dissection in proximity to vasculature. (Benito et al., 2015; Dottino et al., 1999)

The majority of studies that report vascular injury include less than 10 cases. The purpose of this study was to review our experience with major vascular injury during gynecologic cancer surgery in the context of a fellowship training program.

2. Methods

This was a retrospective chart review of women undergoing surgery by our gynecologic oncology department from 7/1/99 to 6/30/20 who had a major vascular injury. All women who underwent gynecologic

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cancer surgery by one of the Moffitt Cancer Center faculty were included. The study was approved by the Moffitt Cancer Center institutional review board. We identified women who sustained a vascular injury by a combination of CPT code and medical record searches, fellow case logs and a list maintained by a Moffitt Cancer Center ongoing quality assurance program. Included were all patients who sustained a major vascular injury. There were no exclusion criteria. For the purpose of this study, major vascular injury was defined as any full-thickness injury (incidental or purposeful) to the major vasculature (aorta, inferior vena cava, iliac vessels, femoral vessels, miscellaneous upper abdominal vessels) that occurred during the course of surgery.

Data collected during the chart review included patient characteristics, diagnosis, procedures, location and mechanism of injury, management of the injury, any change in the planned operation as a result of the injury, and postoperative course including any sequelae of the injury. Data were expressed as median and range for continuous variables and as frequency and percentage for categorical variables. Fisher's exact test was used to analyze differences in complication rates between groups. Statistical analysis was performed using Graphpad Prism.

3. Results

During the years of the study, 52 patients incurred a major vascular injury during 52 surgeries, including seven patients with complex or multiple injuries. This represented an incidence of less than 0.5% of the major cases done during that time period. Patient characteristics, prior treatment, diagnosis and planned procedure(s) are given in Table 1. Location and mechanism of injury, repair and resulting complications are noted in Table 2. Of note there were seven patients with complex injuries or multiple injuries, patients with multiple vascular structures injured concurrently or more than one incident of vascular injury during an operation respectively.

There were 13 arterial injuries (Table 3). Injuries that occurred during adhesiolysis generally involved dissecting densely fibrotic pelvic structures. There were 2 cases of a retractor causing avulsion of the inferior mesenteric artery (IMA) off the aorta; these were managed with suture ligation of each end of the vessel. Also, there was once case of complex injury to the aorta as well as iliac vasculature resulting initially from a direct trocar injury. After immediate conversion to laparotomy and intraoperative consultation to vascular surgery, attempts were made to control the bleeding with clamps, clips, suture repair and finally an interpositional graft. This resulted in a blood loss of at least 7 L and massive transfusion protocol resuscitation that included at least 60 units of PRBCs transfused. All efforts were unsuccessful culminating in intraoperative death.

There were 38 patients with venous injuries including five with complex or multiple injuries (Table 4). Pressure alone was used to manage avulsion of a venule to the IVC and an injury to the IVC caused by a Veres needle. Hemostatic agents were used alone in 2 cases of injury during lymphadenectomy including unidentified venous bleeding and a sharp dissection injury to the external iliac vein. Clips were used obtain hemostasis in 13 cases, including four cases as the only means of management.

A total of 13 patients had vascular injuries at the time of laparoscopic surgery. The median estimated blood loss for patient's undergoing a laparoscopic surgery complicated by vascular injury was 575 mL (100 mL–massive unquantifiable) in all patients, 350 mL in robotic cases and 975 mL in laparoscopic cases. Six out of 13 (46.2%) required blood transfusion at a median of 3 units of packed red blood cells (0–61). Conversion to laparotomy occurred in 8 patients (61.5%) including 1 of 4 (25%) robotic cases and 7 of 9 (77.8%) laparoscopic cases. Fewer cases of venous injury required conversion of laparoscopy for repair compared with arterial injuries, 33.3% (2/6) versus 85.7% (6/7) respectively. Five of the injuries were to the external iliac artery. Three of these occurred during a lymph node dissection, one during superficial entry into the retroperitoneum and the last during dissection of bowel off of the round

Table 1

Shows patients background	characteristics, diagnoses and	l surgeries performed.
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snows patients background chait	Total	Arterial	Venous
Age	59 (30–79)	57.5 (35–72)	59 (39–79)
Age Body Mass Index (BMI)	28.7	31.45	28.86
body wass muck (bwir)	(16.4–49.2)	(24.1–49.2)	(16.4–45)
Prior abdominal surgery	51% (27/52)	54.5% (6/11)	47.4% (18/
(any)	01/0 (27/02)	01.070 (0/11)	38)
Prior hysterectomy	9.62% (5/52)	9.1% (1/11)	7.89% (3/
,			38)
Prior lymphadenectomy	3.85% (2/52)	9.1% (1/11)	2.63% (1/
			38)
Prior Pelvic Radiation	9.62% (5/52)	9.1% (1/11)	10.5% (4/
			38)
Diagnosis			
Ovarian Cancer	28.8% (15/	7.69% (1/13)	28.9% (11/
	52)		38)
Uterine Cancer	40.4% (21/	53.8% (7/13)	39.5% (15/
	52)		38)
Cervical Cancer	19.2% (10/	15.4% (2/13)	21.1% (8/
	52)		38)
Vulvar/Vaginal Cancer	3.8% (2/52)	0.00% (0/13)	5.13% (2/
Description of Discontrol City	1 000/ (1 /50)	0.000/ (0./10)	38)
Recurrent Placental Site	1.92% (1/52)	0.00% (0/13)	2.63% (1/
Trophoblastic Tumor	E 00/ (2/E2)	00.10/ (0./10)	38)
Benign/Preinvasive	5.8% (3/52)	23.1% (3/13)	2.63% (1/ 38)
Procedure*			38)
Pelvic exenteration	7	1	6
Simple Hysterectomy (+/- removal		1	0
Abdominal	20	4	16
Laparoscopic	3	1	2
Robotic	4	2	2
Radical Hysterectomy (+/- remova	al adnexa)		
Abdominal	9	2	7
Laparoscopic	1	0	1
Robotic	0	0	0
Pelvic lymphadenectomy			
Abdominal	23	3	21
Laparoscopic	3	0	3
Robotic	4	2	2
Para-aortic lymphadenectomy			
Abdominal	19	2	18
Laparoscopic	1	0	1
Robotic	1 7	0 2	1 4
Cytoreductive Surgery	/	2	4
Oophorecotmy (without hysterectomy)			
Abdominal	2	1	1
Laparoscopic	0	0	0
Robotic	0	0	0
Intestinal Surgery (not	1	1	0
cytoreductive)	-	-	0
Lysis of Adhesions			
Abdominal	4	1	2
Laparoscopic	2	1	1
Robotic	0	0	0
Diagnostic laparoscopy	4	3	1

ligament. Each of these injuries was repaired with suture and four required conversion to laparotomy. The external iliac artery injury that did not result in conversion to laparotomy occurred during a robotic lymph node dissection and was repaired robotically with suture. There were two injuries to the IVC that occurred during traditional laparoscopic lymphadenectomy; one was successfully repaired laparoscopically with clips and hemostatic agents while the other required conversion to laparotomy and suture repair. There were two robotic cases of injury to the external iliac vein; one occurred during opening of the retroperitoneum while the other occurred during lymphadenectomy. Both were managed robotically with suture and hemostatic agents. Similarly, there was one external iliac vein injury that occurred during laparoscopic lymphadenectomy; this was managed with conversion to laparotomy and suture repair. Avulsion of the IMA off the aorta during retraction for lymph node dissection occurred in one robotic case

Table 2

Shows location and mechanism of injury as well as means of repair. Intraoperative and postoperative complications are show. Percentage of postoperative complications are included for those postoperative course documentation was available.

Location of Injury	Number
Inferior vena cava	32.7% (17/52)
External iliac vein	23.1% (12/52)
External iliac artery	15.4% (8/52)
Complex/Multiple	13.5%(7/52)
Venous - unidentified, lumbar, sacral,	11.5% (6/52)
retroperitoneal	
Common iliac vein	7.69% (4/52)
Inferior mesenteric artery	5.77% (3/52)
Renal vein	3.85% (2/52)
Splenic Hilar vessel	1.92% (1/52)
Saphinous vein	1.92% (1/52)
Obturator Vein	1.92% (1/52)
Mesenteric vessels	1.92% (1/52)
Internal Iliac Vein	1.92% (1/52)
Internal iliac artery	1.92% (1/52)
Femoral Vein	1.92% (1/52)
_ Aorta	1.92% (1/52)
Mechanism of Injury	
Lymph Node Dissection	51.9% (27/52)
Adhesiolysis/dissection of tumor	15.4% (8/52)
Retraction / Avulsion	13.5% (7/52)
Ureterolysis	5.77% (3/52)
Veres/Trocar Entry	3.85% (2/52)
Retroperitoneal Entry	3.85% (2/52)
Skin incision (groin)	1.92% (1/52)
Means of Repair*	
Suture Repair	80.8% (42/52)
Hemostatic agent	28.8% (15/52)
Clip	19.2% (10/52)
Suture Ligation	13.5% (7/52)
Reanastamosis	3.85% (2/52)
Pressure alone	3.85% (2/52)
Splenectomy	1.92% (1/52)
Vascular graft	1.92% (1/52)
Intraoperative Complications	
Estimated Blood Loss	800 cc (100 -
	unquantifiable)
Blood Transfusion	2 (0-61)
Change in Procedure	15.4% (8/52)
Intraoperative Vascular Consultation	21.2% (11/52)
Intraoperative Death	1.9% (1/52)
Postoperative complications	
Postoperative Transfusion	19.6% (9/46)
Venous Thrombolism	19/6% (9/46)

requiring conversion to laparotomy and suture repair. In one case there was injury to the IVC secondary to a Veress needle injury. A small hematoma was noted and pressure was applied; as no expansion was noted no further measures were necessary to achieve control. The final laparoscopic case with vascular injury was a complex injury to the aorta secondary to direct trocar injury. This is described above with arterial injuries.

In one case avulsion of the splenic hilar vasculature occurred during adhesiolysis performed to facilitate omentectomy. This was managed with splenectomy. Also of note was the injury to the femoral vein. The patient had previously been treated with vulvar radiation. She had recurrent vulvar cancer with tumor extending to the thigh. At the time of extensive vulvar resection for during a pelvic exenteration it was noted that there was scarring and tethering of the skin in the groin to the underlying musculature. During the dissection of the skin off this area some additional muscle was resected to obtain a margin. Significant venous bleeding was noted; this was identified to be the femoral vein which was repaired with 5–0 polypropylene suture.

Postoperative complications were similar between patients with arterial and venous injuries. Postoperative transfusions were required in 15.4% (2/13) of patients with arterial injuries and 21.9% (7/22) of

Table 3

Demonstrates the procedure, mechanisms of injury and repair as well as complications specific to arterial injuries.

Procedure			
	Laparoscopy	53.9% (7/13)	
	Laparotomy	38.5% (5/13)	
-	Exenteration	7.69% (1/13)	
Mechan	ism of Injury		
	Resection of mass or lysis of adhesions	30.8% (4/13)	
	Lymphadenectomy	30.8% (4/13)	
	Retraction avulsion	15.38% (2/13)	
	Ureterolysis	7.69% (1/13)	
	Entry into retroperitoneum	7.69% (1/13)	
	Direct trocar injury	7.69% (1/13)	
Mechan	Mechanism of Repair		
	Suture Repair	76.9% (10/13)	
	End-to-end anastamosis	15.4% (2/13)	
	Attempted interpositional graft	7.69% (1/13)	
Median	estimated blood loss	975 mL (250- massive)	
Units of Red blood cells transfused		2 (0-61)	
Intraop	Complications		
	Transfusion	80% (8/10)	
	Conversion to laparotomy	85.7% (6/7)	
	Intraoperative Vascular Consultation	46.15% (6/13)	
	Intraoperative Death	7.69% (1/13)	
Postop	Complications		
	Transfusion	15.38% (2/13)	
	Venous Thromboembolism	7.69% (1/13)	

Table 4

Demonstrates the procedure, mechanisms of injury and repair as well as complications specific to venous injuries.

Procedure		
	Laparoscopy	15.8% (6/38)
	Laparotomy	68.4% (26/38)
	Exenteration	15.8% (6/38)
Mechanism	of Injury	
	Resection of tumor or lysis of adhesions	10.5% (4/38)
	Lymphadenectomy	63.2% (24/38)
	Retraction avulsion	13.2% (5/38)
	Ureterolysis	2.63% (1/38)
	Entry into retroperitoneum	2.63% (1/38)
	Veres Needle Injury	2.63% (1/38)
	Other / Unknown	5.26% (2/38)
Mechanism	of Repair	
	Pressure alone	5.26% (2/38)
	Hemostatic agent(s)	34.2% (13/38)
	Clip	23.7% (9/38)
	Suture	81.6% (31/38)
Estimate Blood Loss (mL)		750 (100-4000)
Units of Red Blood Cells Transfused		1 (0–9)
Intraoperat	tive Complications	
	Transfusion	57.7% (15/26)
	Conversion to laparotomy	33.3% (2/6)
	Intraoperative Vascular Consultation	14.3% (4/28)
	Nerve Injury	2.63% (1/38)
	Death	0% (0/38)
Postop Complications		
	Transfusion	21.9% (7/32)
	Venous Thromboembolism	25.0% (8/32)

patients with venous injuries (p = 0.43). Venous thromboembolism was seen postoperatively in 7.69% (1/13) and 25.0% (8/32) of patients with arterial and venous injuries respectively (p = 0.249).

4. Discussion

Gynecologic oncologists do not receive specialized training in vascular surgery. However, in the course of oncologic resection around major pelvic and paraaortic vasculature, including routine pelvic and paraaortic lymphadenectomy, occasional injury of a major blood vessel is inevitable. Management of such an injury often requires nothing more that pressure without or with hemostatic agents, but in some cases necessitates surgical repair. Gynecologic oncologists experience and receive some training in management of these injuries during fellowship, although the extent to which intraoperative vascular surgery consultation and help is sought is unknown. With a reduction in experience with pelvic and paraaortic lymphadenectomy as well as other types of radical pelvic surgery, trainees will encounter fewer vascular injuries and the range of types of management required. (Hoffman et al., 2019; Hoffman et al., 2020) Surgical simulation training in the management of major vascular injuries has been reported. A live animal is probably the model with best fidelity for this particular training. (Hoffman et al., 2009, 2019)

The pelvic organs drain via the internal iliac venous plexus, a complex and delicate network of veins that progressively coalesce to the short internal iliac vein. Injury to the more cephalad and coalescing part of this plexus is more likely to result in substantial hemorrhage that may be difficult to control due to the caliber, anatomic complexity and relative surgical inaccessibility. Such injury is most likely to occur during resection of obturator lymph nodes but is especially likely during radical resection of a tumor invading this region. Control of bleeding is best done prophylactically. When hemorrhage is encountered, gentle tissue handling is important in order to prevent further injury to the plexus and exacerbation of the problem. Pressure (judiciously), hemostatic agents, suture and clips may all be useful. The obturator nerve and the lumbosacral nerve plexus are in harm's way. In the present study, internal iliac venous plexus injury was reported in only one patient. We suspect that injury of this plexus is under-reported, with disruption of these veins likely being responsible for cases of massive pelvic hemorrhage not identified in this study.

The pelvic organs are nourished by the internal iliac arteries. It is a system with numerous anastamotic channels and redundancy such that sacrifice of even major branches has little consequence (buttock ischemia may occur). In fact, these branches are sometimes tied off or occluded in an effort to control pelvic hemorrhage. Arterial branches are most frequently injured during resection of obturator lymph nodes. Injury to arterial branches are more easily identified than those form the veins but with the same issue of limited surgical accessibility. Resection of tumor invading this region requires prophylactic sacrifice of the involved arteries. In our study, injury was reported in only one patient. Again we think under-reporting is likely as branches of this arterial system are commonly encountered and sometimes injured but in general are easily controlled.

The external iliac vein may also be injured during pelvic lymphadenectomy. Trocar injury of this vein has also been reported. Resection of tumor from the vein is risky and at times the vein must be tied off and/ or resected. A small injury is likely to require pressure only. Suture repair should be perpendicular to the lumen if possible, to avoid constriction. Given its prominent location and thin wall, it is not surprising that this vein was the second most common site of injury in the present series. Although control of bleeding is readily obtained and repair is even feasible without conversion to laparotomy, our experience suggests that these patients are at high risk for subsequent deep vein thrombosis. (Greene et al., 2012; Hoffman and Humphrey, 2011)

The external iliac artery may be injured during pelvic lymphadenectomy, although the thick arterial wall makes this uncommon. Resection of adherent positive nodes or other tumor involving the artery is more problematic. With skill and patience, arteriolysis is often possible (obviously without oncologic margins). In rare cases, resection is considered – preferably with re-establishment of arterial flow. Trocar injury has also been reported. The viability of the lower extremity is at stake and repair should be performed by someone experienced at doing this whenever possible. In our study, this was the third most common site of injury. In all eight cases we were able to promptly recognize the injury and control the bleeding. However, with the exception of one minor laceration repaired robotically, we enlisted the help of a vascular surgeon to perform the repair. The common iliac veins may be injured during lymphadenectomy. Lymph nodes along the right common iliac vein are much more likely to be involved with metastatic disease from gynecologic malignancy. Injury of this vein during lymphadenectomy is commonly the result of shearing of venules entering the vein, which may often be avoided by dissecting cephalad to caudad and meticulous prophylactic control of the venules as they are encountered. The right common iliac vein is also reported to be the most common major vein injured by a trocar. Management of injury is the same as that described for the external iliac vein. The majority of the left common iliac vein crosses the cephalad portion of the presacral space and may be injured during access to this space. The vein runs dorsal to the left common iliac artery to form the inferior vena cava, and access to an injury here can be challenging. In our study four injuries were reported, all during lymphadenectomy and all controlled without significant difficulty.

Injury of the common iliac arteries or aorta is uncommon during gynecologic cancer surgery. Resection of encasing metastatic lymph nodes carries this risk and should be undertaken with consideration of risk versus benefit and proper anticipation of potential major arterial injury. Trocar injury of these structures has been reported. During lymphadenectomy the IMA may be avulsed from the aorta. Traction with a retractor or instrument or direct laceration have all been noted at our centers. Loss of the IMA at this level is rarely of consequence regarding intestinal blood supply due to extensive anastomoses through the mesentery, although this does require clinic evaluation during the case. If the stump of the artery can be secured then the problem is resolved. Suture repair of a small hole in the aorta may be necessary. In the present series two aortic injuries were reported, one of these being the intraoperative death. The other injury was the result of avulsion of the IMA at its origin during lymphadenectomy. Such injuries must be emergently controlled and repaired with suture.

The inferior vena cava is most commonly injured during a right paraaortic lymphadenectomy, again by shearing of draining venules. Prevention and management are the same. Trocar injury has also been reported. Distal and proximal control as well as repair are approached with caution to avoid exacerbating a tear of this rather delicate vein wall. Sponge sticks, Allis clamps, Statisnsiky vascular clamps and Bulldog clamps are all potentially useful. In our study this was the most common site of injury. Any defect beyond a very small (less than 1–2 mm) injury that is readily controlled and resolved with pressure (with or without hemostatic agents) probably deserves suture repair, although some advanced (and expensive) hemostatic products exist that are reported to repair a larger hole. (Allotey et al., 2020)

Given the potential complexity of repair, the potential for rapid exsanguination and the risk to the lower extremity, it is the opinion of the authors that the majority of major arterial injuries (aorta, common iliac, external iliac) should be repaired by a vascular surgeon whenever possible. Injury to a major vein is generally manageable by a gynecologic oncologist, with liberal use of vascular surgery consultation at their discretion. Following repair of a major venous injury and stabilization of the patient, consideration should be given to anticoagulation for at least several weeks (6 months if stenosis is likely).

Controlling (and potentially resolving) venous bleeding with pressure (with or without hemostatic agents) is feasible with straight-stick laparoscopy and should at least be briefly attempted if proceeding with laparotomy. Laparoscopic vascular suture repair, however, is beyond the skill set of most surgeons. However, the daVinci robotic platform allows for excellent visualization and precise suturing together with the potential for obtaining proximal and distal control of a major vascular injury. Expert surgical skill and bedside assistance are necessary, together with preparation without hesitancy for immediate conversion to laparotomy. In our series this was accomplished successfully for two external iliac vein lacerations and one minor external iliac artery laceration.

A strength of this study is the relatively large sample size reviewing vascular complications. Another strength is the breakdown by location,

mechanism of injury, repair and outcome. Weaknesses are those common to retrospective studies. Precise mechanism of injury, of obvious interest, would be best determined at time of surgery rather than through review of records. Likely there were cases that were not identified using CPT codes if a diagnosis of vascular injury was not separately documented. Additionally, not all information was available for all patients.

Vascular injury remains a rare but potentially morbid complication of gynecologic oncologic surgery. Here we report lymph node dissection as the most common time for a vascular injury to occur, thus, the external iliac vein and IVC as most common sites of injury. Prompt recognition and management are imperative in minimizing persistent bleeding and complications. If injury occurs during minimally invasive surgery, small venous injuries can frequently be managed with pressure and hemostatic agents; larger or arterial injuries may be managed with suture repair with appropriate expertise in robotic or laparoscopic suturing.

Conflict of Interest Statement

Dr. Wenham reports personal fees from Genentech, personal fees from Legend Therapeutics, personal fees from Regeneron, personal fees from GSK, personal fees from Clovis, personal fees from Astra Zeneca, personal fees from Tesaro, grants and personal fees from Merck, other from Marker Therpeutics, personal fees from Ovation Diagnostics, outside the submitted work. The remainder of the authors have nothing to disclose.

CRediT authorship contribution statement

Andrea L. Buras: Investigation, Formal analysis, Visualization, Writing - original draft. Jing Yi Chern: Writing - review & editing. Hye Sook Chon: Writing - review & editing. Mian M. Shahzad: Writing review & editing. Robert M. Wenham: Writing - review & editing. Mitchel S. Hoffman: Conceptualization, Supervision, Writing - original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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