

Comparison of four transdiaphragmatic approaches to remove cavoatrial tumor thrombi: a pilot study

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Introduction Surgical treatment of kidney cancer with a tumor thrombus spreading through the inferior vena cava (IVC) up to the right atrium remains a challenge.

The aim of this article was to 1. assess the safety and feasibility of four transdiaphragmatic surgical approaches to the right atrium from the abdominal cavity; 2. to evaluate the feasibility of palpation and displacement of thrombi below the diaphragm.

Material and methods Four cadaveric specimens preserved with the Thiel method to assess each surgical access: 1) extrapericardial T-shaped diaphragmotomy, 2) extrapericardial T-shaped + circular diaphragmotomy, 3) transpericardial T-shaped diaphragmotomy with longitudinal pericardiectomy, 4) transpericardial T-shaped + circular diaphragmotomy with longitudinal and circular pericardiectomy. Different diameters and density of tumor thrombus simulators, placed at various levels from the cava-diaphragm junction, were used to evaluate the palpation and displacement of the thrombus. Two surgeons performed each assessment independently.

Results Approaches 2, 3 and 4 were significantly better than approach 1, regarding the feasibility of palpation, according to both surgeons (surgeon 1 Chi-square 21.56, $p = 0.001$; surgeon 2 Chi-square 27.83, $p < 0.0001$). Approach 1 also showed a significant higher number of impossible displacements recorded by both surgeons (surgeon 1 Chi-square 19.02, $p = 0.004$; surgeon 2 Chi-square 20.01, $p = 0.003$). Only surgeon 1 recorded a significant lower number of easy palpations at 4 cm from the cava-diaphragm junction (Chi-square 14.10, $p = 0.007$). There were no high-risk complications in any approach.

Conclusions The transdiaphragmatic access to the right atrium from the abdominal cavity is feasible using three of the four surgical approaches. They are an adequate alternative to sternotomy.

Key Words: inferior vena cava ↔ tumor thrombus ↔ right atrium
↔ transdiaphragmatic surgical approaches

INTRODUCTION

A characteristic feature of renal cell carcinoma is the penetration of the renal venous vessels with the formation of a tumor thrombus [1]. Surgical treatment of kidney tumors with a tumor thrombus spreading through the inferior vena cava (IVC) lumen above

the diaphragm up to the right atrium remains a challenge [2, 3]. The standard surgical approach to tumor thrombus removal entails sternotomy, cardiopulmonary bypass with or without circulatory arrest and deep hypothermia and is associated with a high morbidity and mortality rate [4]. However, less traumatic surgical approaches, like the liver

transplantation technique, have emerged in recent years [4–10]. The liver transplantation technique includes some elements of orthotopic liver transplantation without using extra corporal circulation. These elements are liver mobilization, access to the supradiaphragmatic part of the IVC through the diaphragm from the abdominal cavity, and manual displacement of the tumour thrombus below the diaphragm and the major hepatic veins: a procedure named ‘milking maneuver’ [8, 9, 11–16] [17, 18]. Despite the growing interest in this method, it is currently rarely used due to the lack of data regarding the efficacy and safety of a mediastinal surgical access from the abdominal cavity. Additionally, it remains unclear which thrombus dimension and density inside the atrium are suitable to be treated with a thrombectomy that employs the ‘milking maneuver’.

This study evaluates the feasibility and safety of four transdiaphragmatic accesses to the supradiaphragmatic IVC and right atrium from the abdominal cavity, including a novel transpericardial approach developed by our group: T-shaped + circular diaphragmotomy with longitudinal and circular pericardiotomy. We also assessed the feasibility of palpation and displacement below the diaphragm of floating tumor thrombi of various diameters and densities, reaching different levels, using the ‘milking maneuver’.

MATERIAL AND METHODS

Study population

Four cadaveric specimens preserved with the Thiel method [19, 20]: 3 males (76, 78, and 88 years of age) and 1 female (93 years old). Cases with a body mass index lower than 19 and higher than 28, and with a history of previous sternotomy were excluded. Only one case had a previous history of abdominal laparotomy that did not preclude the procedures of this project and was then included. The preparation of the bodies was done at the anatomy laboratory of the University of Québec in Trois-Rivières. The study was approved by the Sub-Committee of Ethics of the teaching and research laboratory in anatomy of the university.

Surgical technics

We performed four distinct surgical approaches, one per body specimen:

- 1) T-shaped diaphragmotomy
- 2) T-shaped + circular diaphragmotomy
- 3) T-shaped diaphragmotomy with longitudinal pericardiotomy

- 4) T-shaped + circular diaphragmotomy with longitudinal and circular pericardiotomy

The first three approaches have been used by other groups before [3–8, 11, 12, 18]. We included a fourth approach, developed by our group [21], for the treatment of intra-cava floating thrombi.

After a chevron laparotomy, we performed a liver mobilization of the ‘piggy-back’ type [2, 5, 7, 11, 13, 16, 22], as well as IVC mobilization at the level of the suprahepatic infra-diaphragmatic segment.

In the first body, an extrapericardial transverse incision of the diaphragm was carried out parallel to the anterior semi-circle of the IVC with a margin of 3–5 mm, which was supplemented by a perpendicular longitudinal incision within 3–4 cm (approach 1: T-shaped diaphragmotomy, Figure 1A). In the second body, a total circular isolation of the IVC from the diaphragm without opening the pericardium (approach 2) was added to the extrapericardial T-shaped diaphragmotomy (Figure 1B). The incision area was 1–2 mm from the IVC surface to avoid damage to the right phrenic nerve. In the third body, a combination of extrapericardial T-shaped diaphragmotomy with longitudinal incision of the pericardium within 4–5 cm was performed (approach 3, Figure 1C and Figure 2). Finally, in the fourth body we used our approach [21], providing wide access to the entire right atrium from the abdominal cavity. It included a combination of extrapericardial T-shaped with circular diaphragmotomy and longitudinal opening of the pericardium within 4–5 cm. Then we continued the pericardial incision around the anterior, right and posterior surfaces of the intrapericardial IVC (approach 4, Figure 1D and Figure 2). In all cases, after reaching the supradiaphragmatic area, we passed a tourniquet around the cavoatrial junction and performed palpation of the right atrium. Once the surgical procedures were completed, we performed a thoracotomy between the second and fifth intercostal spaces to create a fenestration that would allow the assessment of signs of injury to the right phrenic nerve and parietal pleura, thanks to the exposure of the thoracic surface of the right diaphragm and pericardium in the area of the right atrium.

Palpation and displacement technic

To determine the possibility of palpation of the tumor thrombus apex using the thumb, index, and middle fingers (‘milking maneuver’) we used tumor thrombus simulators (TTS) of different diameters (7 mm, 12 mm and 20 mm) and density (solid-category ‘sausage’ and soft-category ‘porridge’). The solid thrombus models were made of silicone and the soft models of buoyant polyethylene foam. All TTSs were marked with a scale in centimeters and had a length of 30 cm.

After performing each of the four approaches, we performed a longitudinal 3 cm long incision in the subhepatic segment of the IVC and introduced the TTSs into its lumen reaching the junction of the IVC and diaphragm (cava-diaphragm junction). From this point we displaced the TTS 2 cm, 3 cm and 4 cm above the level of the junction, simulating a floating thrombus that progressively

reaches higher levels. Then, we aimed the palpation of the thrombus apex and the displacement of the whole thrombus from the apex at all the different levels. The goal was to always perform the displacement from the apex to prevent a fragmentation and embolization of the thrombus that could arise by palpation and displacement of the body of the thrombus.

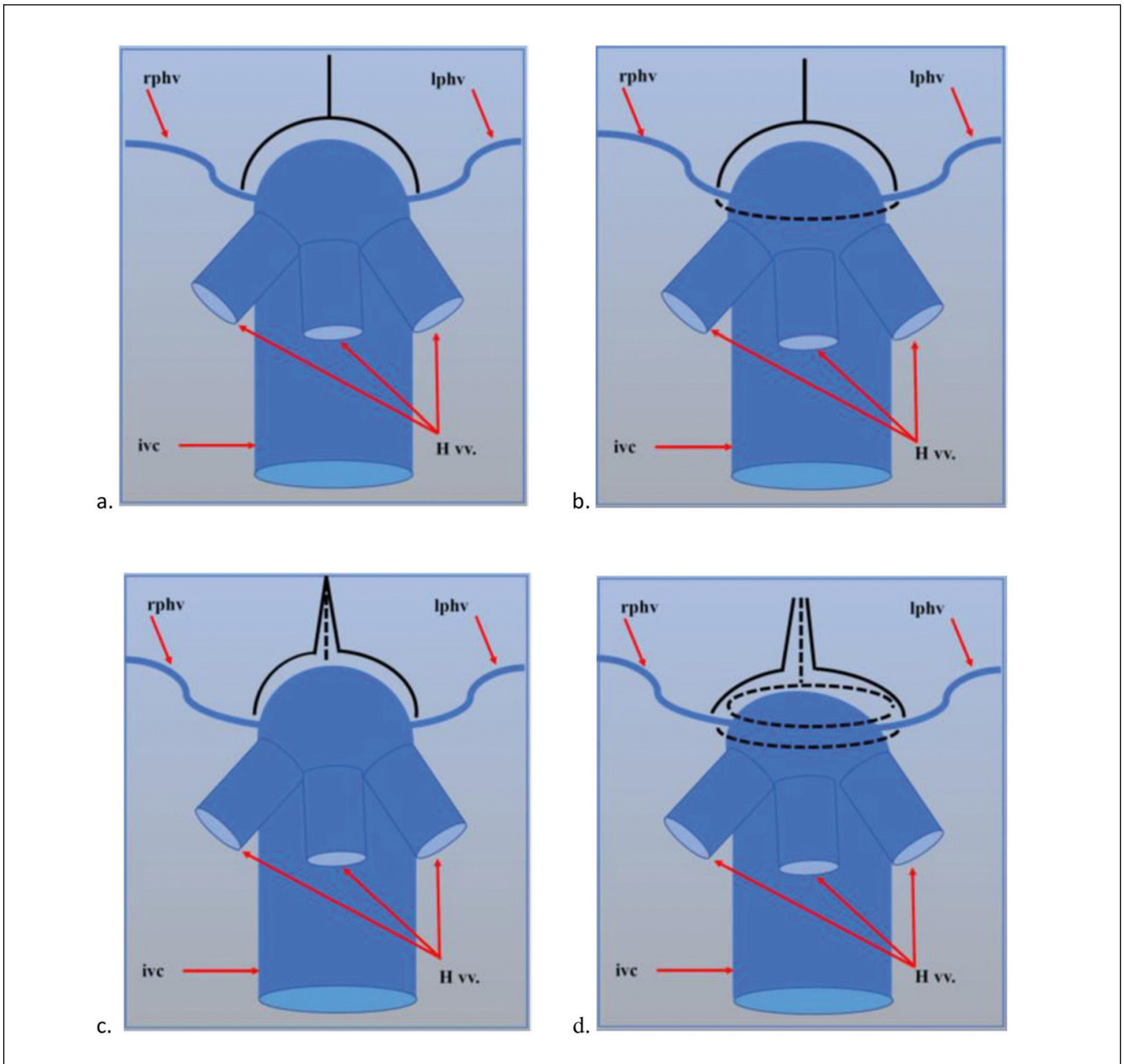


Figure 1. Schematic representation of accesses 1, 2, 3, 4 (view from the abdominal cavity): **a.** Extrapericardial T-shaped diaphragmotomy; **b.** Extrapericardial T-shaped + circular diaphragmotomy; **c.** T-shaped diaphragmotomy with longitudinal pericardiotomy; **d.** T-shaped + circular diaphragmotomy with longitudinal and circular pericardiotomy.

rphv – right phrenic vein; lphv – left phrenic vein; ivc – inferior vena cava; H vv. – hepatic veins

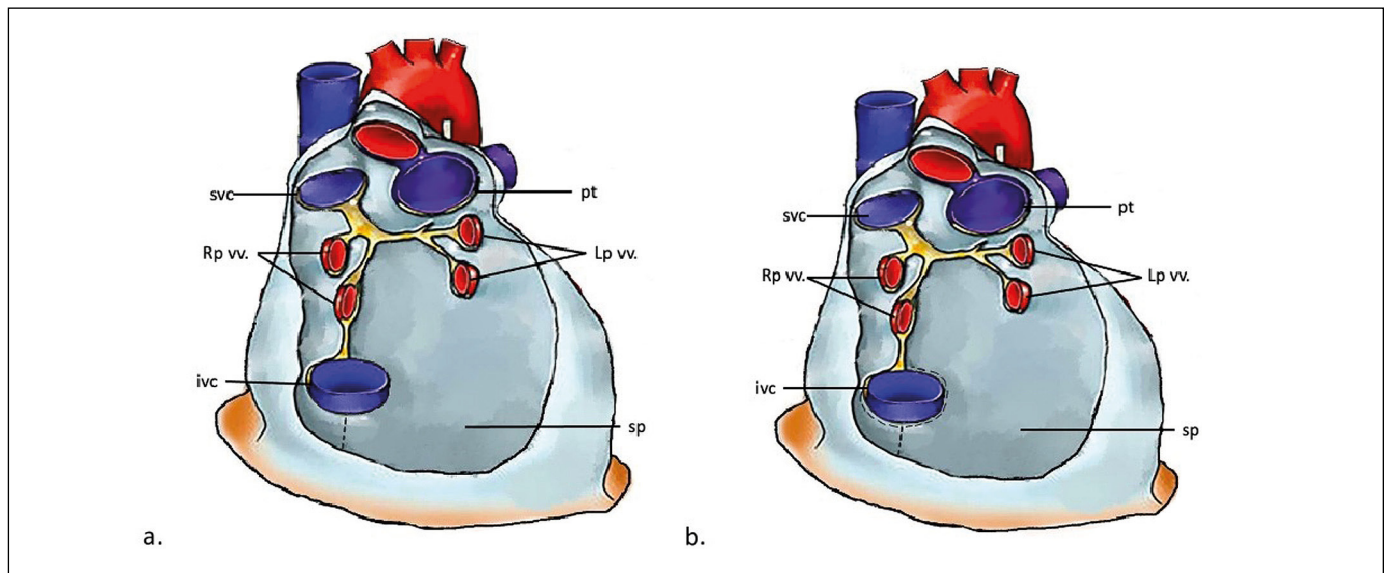


Figure 2. Schematic representation of accesses 3, 4 (view from the chest cavity): **a.** Longitudinal pericardiotomy; **b.** Longitudinal and circular pericardiotomy.

svc – superior vena cava; pt – pulmonary trunk; Rp vv. – right pulmonary veins; Lp vv. – left pulmonary veins; ivc – inferior vena cava; sp – serous pericardium

Palpation feasibility scale

The ability to perform the palpation of the TTS was evaluated with the following scale:

- 1) easy: successful apex palpation at the first try with a superior approach (fingers reach directly the level above the apex through the vessel wall);
- 2) difficult: palpation of apex after palpatory search by climbing the surface of the vessel where the thrombus is perceived, which implies the risk of thrombus fragmentation; and
- 3) impossible: apex never reached.

Displacement feasibility scale

The ability to displace the thrombus caudally ('milking maneuver') allowing its extraction was assessed using the following scale:

- 1) easy: the thrombus slid spontaneously upon minimal pressure on the apex;
- 2) difficult: the thrombus did not slide spontaneously upon touching the apex and had to be gently squeezed out of the IVC;
- 3) impossible: displacement was not achievable, or the thrombus could be displaced using vigorous squeezing maneuvers, which would lead to fragmentation.

Anatomic complications scale

We performed an assessment of the techniques based on the number and type of anatomic complications, stratifying three levels.

The level of complications was graded as

none: 0 points;

low-level: 1–3 points; and

high-level: >3 points.

The anatomic complications included in our scale are presented in Table 1.

The scoring of the anatomic complications was done as a consensus of four surgical experts, the two surgeons who performed the procedure, including the implementation of 4 approaches, an assessment of the possibility and safety of palpation and displacement of TTS (I.Z. and A.N., experience in abdominal surgery 25 and 16 years, respectively; additionally, 1 and 3 years of experience in a hepatic transplant and uro-oncologic unit); and two surgeons who evaluated the recording of the procedure (video assess-

Table 1. Parameters of complications in points

| Intraoperative damages | Points |
|---------------------------------|--------|
| No injury | 0 |
| Liver | 1 |
| Major hepatic veins | |
| Grade I: vascular defect <3 mm | 1 |
| Grade II: vascular defect >3 mm | 2 |
| Inferior vena cava | |
| Grade I: vascular defect <3 mm | 1 |
| Grade II: vascular defect >3 mm | 2 |
| Right parietal pleura | 1 |
| Right phrenic nerve* | 2 |

*We scored the right phrenic nerve with 2 given the seriousness of this injury, which entails longstanding consequences for the health of the patient

ment: D.S. and M.J., experience in abdominal surgery and urology 29 and 11 years, respectively).

Statistical analysis

Differences in palpation and displacement feasibility, in relation to four separate variables: 1) surgical approach, 2) TTS level, 3) TTS diameter, and 4) TTS density, were assessed using the Chi-square test, correcting for multiple comparisons (Bonferroni) [23]. Differences between the surgeons who performed the measurements were assessed using Cohen's kappa coefficient.

Ethical considerations

This project was performed on human bodies obtained from donors by their lifetime written consent. In 2019 our project was approved by the Research Ethics Board of our University and by an ethics sub-committee of the anatomy teaching and research laboratory: Ethics Certificate Number: SCELERA-19-06.

RESULTS

We performed a total of 72 assessments of feasibility and anatomic complications. In each body we used 2 types of TTS (soft and solid) with three different diameters (total of 6 TTS), placing each at three different levels (2, 3 and 4 cm), completing 18 different

measurements per body/approach, as if we were assessing 18 kidney cancer cases with tumor thrombi. The feasibility scores for palpation and displacement of the thrombi in relation to surgical approach, and level, density and diameter of the thrombi are presented in Tables 2 and 3.

Regarding the palpation of the TTSs in relation to the surgical approach, the extrapericardial T-shaped + circular diaphragmotomy (approach 2) and the two transpericardial approaches (3 and 4) were significantly better than the extrapericardial T-shaped diaphragmotomy (approach 1), which showed a significantly lower number of easy palpations and a higher number of difficult and impossible palpations, for both surgeons, after Bonferroni correction for multiple comparisons (surgeon 1: Chi-square 21.56, $p = 0.001$; surgeon 2: Chi-square 27.83, $p < 0.0001$). Regarding the palpation in relation to the level of TTSs, only surgeon 1 recorded a significant lower number of easy palpations at 4 cm (Chi-square 14.10, $p = 0.007$). There were no significant differences in palpation at the levels of 2 cm and 3 cm, and there were no significant differences at any level for surgeon 2.

Finally, there were no significant differences in palpation in relation to the density or diameter of the TTSs, for both surgeons.

Considering the feasibility of displacing the thrombus in relation to the surgical approach, only the approach 1 exhibited a significant higher number

Table 2. Feasibility results for thrombi palpation in relation to the surgical approach, level, density and diameter of the thrombus

| Surgical approach | Easy | | Difficult | | Impossible | |
|-------------------|-------------|------------|------------|------------|------------|-----------|
| | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| Approach 1 | 9* (50%) | 8* (44.4%) | 6* (33.3%) | 5* (27.8%) | 3* (16.7%) | 5*(27.8%) |
| Approach 2 | 16 (88.9%) | 17 (94.4%) | 2 (11.1%) | 1 (5.6%) | 0 | 0 |
| Approach 3 | 18 (100%) | 18 (100%) | 0 | 0 | 0 | 0 |
| Approach 4 | 17 (94.4%) | 17 (94.4%) | 1 (5.6%) | 1 (5.6%) | 0 | 0 |
| Levels | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| 2 cm | 24 (100%) | 23 (95.8%) | 0 | 1 (4.2%) | 0 | 0 |
| 3 cm | 21 (87.5%) | 21 (87.5%) | 3 (12.5%) | 2 (8.3%) | 0 | 1 (4.2%) |
| 4 cm | 15* (62.5%) | 16 (66.7%) | 6 (25%) | 4 (16.7%) | 3 (12.5%) | 4 (16.7%) |
| Density | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| Soft | 30 (83.3%) | 28 (77.8%) | 4 (11.1%) | 5 (13.9%) | 2 (5.6%) | 3 (8.3%) |
| Solid | 30 (83.3%) | 32 (88.9%) | 5 (13.9%) | 2 (5.6%) | 1 (2.8%) | 2 (5.6%) |
| Diameter | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| 7 mm | 21 (87.5%) | 19 (79.1%) | 2 (8.3%) | 4 (16.7%) | 1 (4.2%) | 1 (4.2%) |
| 12 mm | 20 (83.3%) | 18 (75%) | 3 (12.5%) | 3 (12.5%) | 1 (4.2%) | 3 (12.5%) |
| 20 mm | 19 (79.1%) | 21 (87.5%) | 4 (16.7%) | 2 (8.3%) | 1 (4.2%) | 1 (4.2%) |

*statistical significance after Bonferroni correction

Table 3. Feasibility results for thrombi displacement in relation to the surgical approach, level, density and diameter of the thrombus

| Technique | Easy | | Difficult | | Impossible | |
|------------|-------------|-------------|-----------|------------|------------|------------|
| | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| Approach 1 | 10 (55.5%) | 10 (55.5%) | 3 (16.7%) | 3 (16.7%) | 5* (27.8%) | 5* (27.8%) |
| Approach 2 | 14 (77.8%) | 13 (72.2%) | 4 (22.2%) | 5 (27.8%) | 0 | 0 |
| Approach 3 | 17 (94.4%) | 17 (94.4%) | 1 (5.6%) | 1 (5.6%) | 0 | 0 |
| Approach 4 | 16 (88.9%) | 13 (72.2%) | 2 (11.1%) | 5 (27.8%) | 0 | 0 |
| Level | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| 2 cm | 23 (95.8%) | 22 (91.7%) | 1 (4.2%) | 2 (8.3%) | 0 | 0 |
| 3 cm | 20 (83.3%) | 19 (79.2%) | 4 (16.7%) | 4 (16.7%) | 0 | 1 (4.2%) |
| 4 cm | 14* (58.3%) | 14 (58.3%) | 5 (20.8%) | 6* (25.0%) | 5 (20.8%) | 4 (16.7%) |
| Density | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| Soft | 25 (69.4%) | 23 (63.9%) | 8 (22.2%) | 10 (27.8%) | 3 (8.3%) | 3 (8.3%) |
| Solid | 32 (88.9%) | 32* (88.9%) | 2 (5.6%) | 2* (5.6%) | 2 (5.6%) | 2 (5.6%) |
| Diameter | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 | Surgeon 1 | Surgeon 2 |
| 7 mm | 20 (83.3%) | 18 (75%) | 2 (8.3%) | 5 (20.8%) | 2 (8.3%) | 1 (4.2%) |
| 12 mm | 18 (75%) | 17 (70.8%) | 4 (16.7%) | 4 (16.7%) | 2 (8.3%) | 3 (12.5%) |
| 20 mm | 19 (79.1%) | 18 (75%) | 4 (16.7%) | 5 (20.8%) | 1 (4.2%) | 1 (4.2%) |

*statistical significance after Bonferroni correction

of impossible displacements as recorded by both surgeons (surgeon 1 Chi-square 19.02, $p = 0.004$; surgeon 2 Chi-square 20.01, $p = 0.003$).

When assessing the displacement in relation to the level, only surgeon 1 recorded a significant lower number of easy displacements and higher number of impossible displacements at 4 cm (Chi-square 14.81, $p = 0.005$). There were no significant differences in displacement of the thrombi in relation to the level for surgeon 2.

Regarding the displacement of the thrombus in relation to the TTS density, there were no significant differences for surgeon 1, but there were for surgeon 2, with a significant higher number of easy displacements and lower number of difficult displacements for the solid TTS type.

Finally, there were no significant differences in the displacement in relation to the TTS diameter for any of the surgeons.

There were no anatomic complications using the extrapericardial approaches, and only grade I vascular damage and liver damage using the transpericardial approaches. All lesions were located at the level or below the diaphragm and were accessible to perform a satisfactory surgical repair. Damages to the right phrenic nerve and right parietal pleura were not detected in any of the cases.

The inter-surgeon (inter-rater) reliability was assessed using the Cohen's-kappa coefficient, which is a measurement ranging from 0: no agreement to 1: perfect agreement. The scores were 0.64 for the palpation and 0.75 for displacement.

DISCUSSION

Extra corporal circulation and hypothermic circulatory arrest are traditional surgical strategies in patients with floating cavoatrial tumor thrombi [4]. However, this approach significantly increases the length of the surgery, requires sternotomy, and is accompanied by complications, such as coagulopathy, neurological disorders, multisystem failure, sternal pain syndrome, mediastinitis and pericardial scar adhesions [4]. The mortality rate in cases of thrombectomy, using cardiopulmonary bypass with or without circulatory arrest, may reach 10% [4]. Currently, alternative surgical methods, which do not use extracorporeal circulation, have begun to develop. One of them is the transplantation technique of thrombectomy, which includes liver mobilization, access to the supradiaphragmatic IVC through the diaphragm from the abdominal cavity and manual displacement of the tumour thrombus below the diaphragm, namely the 'milking maneuver'. This surgical technique is actively used to remove floating tumor thrombi reaching the retro-hepatic and intrapericardial IVC. However, in patients with floating cavoatrial thrombi this technic has not yet been studied. Only a few case reports on this issue have been presented in the literature giving successful results [5, 7, 11, 22, 24, 25].

Our study assessed the feasibility of four different accesses to the right atrium from the abdominal cavity to perform the 'milking maneuver' using various di-

ameters, densities and levels of TTSs. Although our study includes a small number of cases, it allowed us to draw some preliminary conclusions regarding the limitations of one particular approach: the T-shape extrapericardial technique (approach 1), which gave the worst results for both palpation of the floating thrombus apex and its displacement using the 'milking maneuver', as recorded by both surgeons. The other technics, including our novel transpericardial approach, seem to perform equivalently, giving the possibility to palpate and displace the thrombus in all instances. However, a higher number of cases is needed to unveil subtler numerical differences across the three approaches (2, 3, and 4).

The other significant finding was related to the level of the thrombus for the ease of palpation and displacement. Interestingly, only surgeon 1 obtained significantly different results for thrombi at 4 cm, recording a lower rate of easy palpation and displacement and a higher rate of impossible displacement. Surgeon 2 did not record any significant differences. We speculate that these findings could be related to the size of the surgeons' hands, giving surgeon 2 (smaller hands than surgeon 1) the possibility to reach a higher level with less difficulty than surgeon 1.

Finally, there were also differences across surgeons regarding the ease of displacement in relation to the thrombus's density, with surgeon 2 obtaining significantly worse results for soft thrombi. Once again, we hypothesize that the finger's diameter of surgeon 2 (smaller than surgeon 1) could explain the difficulty controlling the apex of a soft thrombus, while a larger finger could fully cover the surface of the apex, regardless of the density.

We also assessed the number of anatomical complications in each surgical approach. None of the technics had high-risk complications. The extrapericardial approaches (1 and 2) did not have any complications, and the transpericardial (3 and 4) only showed low-level incidents. Once again, the low number of cases precludes any significant conclusion at this point. However, the qualitative assessment of the surgeons is that circular mobilization of the cavoatrial junction was more difficult to perform because there is the risk of damage of the posterior wall of IVC. They also noted that the most frequent type of the damage was small caval injuries, although, given the small size of the lesion a high-volume hemorrhage would not be expected. Finally, all lesions were local-

ized at the level or below the diaphragm, so a proper access for suturing was always possible.

A limitation of our work is that the surgical procedures were done on embalmed cadavers using the Thiel fixation method. Specifically, this embalming technic changes the elasticity of the tissues, particularly the muscle, hence the diaphragm, which is a key barrier in our surgical approach. This could imply that, if the extrapericardial approach 1 is less effective in Thiel cadavers, it could be even worse in vivo, due to the extra resistance and tonus of the diaphragm. However, in real surgeries the tonus is also somewhat decreased by the use of myorelaxant, so the limitation of the muscular tonus could be less relevant. Likewise, the lack of muscular tonus could also be partially overestimating the ease of palpation and displacement of all the other approaches.

Finally, in real clinical practice, the surgeon's sensations during palpation of the thrombus and the success of the 'milking maneuver' are influenced by other additional factors, such as the heartbeat, the presence of blood flow in the IVC and in the right atrium. Specifically, the blood flow might complicate preferentially the palpation of soft thrombi, which in real practice could translate into a more favorable outcome for solid thrombi than what we have captured with our ex-vivo experiment.

For the development of this surgical technique, further anatomical and clinical research is needed on a larger sample.

CONCLUSIONS

Transdiaphragmatic access to the right atrium from the abdominal cavity is feasible using three different surgical technics: extrapericardial T-shaped + circular diaphragmotomy, transpericardial T-shaped diaphragmotomy with longitudinal pericardiotomy, and transpericardial T-shaped + circular diaphragmotomy with longitudinal and circular pericardiotomy. They are an adequate alternative to sternotomy. The success of floating thrombus apex palpation and displacement using the 'milking maneuver' seems to be related in part to the level and density of the thrombi, but this could also be dependent on the surgeon.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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