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Review Article

Tumour Thrombi in the Suprahepatic Inferior Vena Cava: The Cardiothoracic Surgeons' View

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Background. Retroperitoneal tumours propagate intrathoracic caval tumour thrombi (ICTT) of which we consider two subgroups: ICTT-III (extracardiac) and ICTT-IV (intracardiac). *Methods*. Case series review. *Results*. 29 series with 784 patients, 453 with extracardiac and 331 with intracardiac ICTT. Average age was 59 years. 98% of the tumours were RCC, 1% adrenal and Wilms' tumours, and 1% transitional cell carcinomas. The prevalent incision was rooftop with or without sternotomy. Mortality was 10% (5% for ICTT-III, 15% for ICTT-IV). Morbidity was 56% (36% for ICTT-III, 64% for ICTT-IV) and reoperation for bleeding was the commonest complication (14%). Mean Blood loss was 2.6 litres for ICTT-III and 3.7 litres for ICTT-IV. Mean blood product use was 2.4 litres for ICTT-III and 3.5 litres for ICTT-IV. Operative and anaesthetic times exceeded 5 hours. Hospital stay averaged 13 days. Variations in perioperative care included preoperative embolisation, perioperative transoesophageal echo, surgical incisions, and extracorporeal circulation. *Brief Summary*. Surgery for ICTT has high transfusion, operating/anaesthetic time, and in-hospital stay requirements, and intracardiac ICTT also attract higher risk. Preoperative tumour embolisation is controversial. The cardiothoracic team offers proactive optimisation of blood loss and preemptive management of intracardiac thrombus impaction: we should always be involved in the management the ICTT.

1. Introduction

Tumour thrombus, as opposed to bland (i.e., blood) thrombus, is a collective term for intravascular metastases with thrombotic elements. Tumour thrombi propagate in the Inferior Vena Cava (IVC) from retroperitoneal primaries such as renal cell carcinoma (RCC). 10% of the 50,000 RCC diagnosed internationally every year [1] present with IVC thrombosis [2]. Similar caval tumour thrombi are found in less common retroperitoneal primaries such as Wilms' tumour [3] and various adrenal, uterine, and bladder tumours. The Levels of tumour thrombi have been defined by Neves and Zincke of Mayo Clinic [4].

Level I, extension into the renal vein;

Level II, extension into the infrahepatic IVC;

Levels III, IVC, extension to the level of hepatic veins but below the diaphragm; and

Levels IV, IVC, extension above the diaphragm and into the right atrium or beyond.

This classification (not to be confused with the MAYO scoring system for metastases) has been more or less established in the literature with small minutiae in definitions [5–8].

Aggressive surgical resection has been the treatment of choice. In RCC, this usually necessitates radical ipsilateral nephrectomy [4–16].

As a whole, the management from the general and urological points of view has recently been reviewed [6, 7, 9], yet the role of the cardiothoracic team can be further discussed specifically in the 1% that tumour thrombi extend into the intrathoracic (supradiaphragmatic and suprahepatic) IVC [2]

These intrathoracic caval tumour thrombi (ICTT) pose an even more complex surgical problem [5].

In search of anatomical boundaries to guide the complex bicoelomic radical resection, we consider hereby two ICTT

TABLE 1: Intrathoracic Caval Tumour Thrombi, cumulative perioperative data from 29 series: Apart from the numbers of ICTT-III and ICTT-IV, values are average.

	Total	ICTT-III	ICTT-IV
N	784	453	331
Age	59	52	56
Gender			
Male	62%	70%	53%
Female	38%	30%	43%
Primary Tumour Side			
Right	64%	76%	54%
Left	36%	24%	46%
Histology			
Renal Cell Carcinoma	98%	99%	98%
Wilms or, Adrenal	1%	1%	1%
Transitional L Cell Carcinomas	1%	0%	1%
Pre-embolisation strategies	29%	22%	30%
Echo studies	88.50%	83.50%	89%
Incision			
Midline Laparotomy	11%	16%	2%
Midline Laparotomy	26%	20%	38%
+ Sternotomy	2070	2070	3070
Thoracoabdominal	3%	4%	6%
Chevron	34%	51%	8%
Chevron + Sternotomy	27%	9%	46%
IVC Resection and graft	12%	5%	19%
IVC clamps			
Partial	22%	22%	21%
Complete	57%	71%	32%
Piggy-back' Liver	62%	72%	40%
Pringle Manoeuver	59%	60%	40%
Perfusion Strategies			
None	51%	84%	12%
Cardiopulmonary Bypass without Arrest	44%	10%	84%
Circulatory Arrest	35%	10%	59%
Venous bypass	5%	6%	4%
Cardiopulmonary Bypass times	103 min	88 min	106 min
Circulatory Arrest times	25 min	23 min	26 min
Procedure duration	358 min	339 min	378 min
Anaesthesia time	362 min	331 min	396 min
Estimated blood Loss	3190 mL	$2665\mathrm{mL}$	$3724\mathrm{mL}$
Volume of Transfusion	$3142\mathrm{mL}$	2404mL	$3548\mathrm{mL}$
Mortality	10%	5%	15%
Morbidity	56%	36%	64%
Haemorrhage and reoperation	14%	9%	26%
Deep venous Thrombosis	2%	1%	1%
Pulmonary Embolism	3%	2%	5%
Myocardial Infarction	1%	3%	0
Dysrhythmias	2%	2%	2%
Abdominal complications	5%	10%	6%

Table 1: Continued.

	Total	ICTT-III	ICTT-IV
Sepsis/Infectious complications	4%	4%	6%
Acute Renal Failure	4%	4%	6%
Any other complications	3%	4%	5%
Length of Hospital Stay	13	14	13

subgroups mirroring the Levels III and IV of the comprehensive "Neves and Zincke" classification [4]: ICTT-III and ICTT-IV, respectively.

We sought the perioperative evidence on ICTT surgery with curative intent. We reflected on relevant data as we sought to define the role of the cardiothoracic surgeon as a member of the multidisciplinary team.

2. Materials and Methods

Ethical issues were not raised; therefore, ethical approval was not sought. Absence of conflict of interest is declared.

2.1. PubMed Search. For clinical studies with at least 10 patients published between 1965 and March 31, 2011 in English, search keywords "cava*" AND "bypass" AND "nephrectomy" were limited to "human subjects." Articles were also identified using the function "related articles" in PubMed and cross-validated by hand search so that overlapping cohorts were appropriately merged. We reanalysed pooled data from these studies. The data were thus tabulated (Table 1) in order to formulate our cohortial endpoints.

2.2. Perioperative Considerations

- (i) Imaging.
 - (a) Echocardiography: in addition to abdominal ultrasound (standard imaging modality for RCC), nine tenths of the cohort had pre- or perioperative cardiac ultrasound (echo) with an increasing use of transoesophageal modality (TOE or TEE). The benefit from TOE is realtime assessment of potentially mobile tumour thrombi in risk of intracardiac impaction, when preemptive use of extracorporeal perfusion is indicated.
 - (b) Embolisation of the (renal) tumour through angiography/cavography. The embolisation aims primarily to limit vascularity and thence haemorrhage upon surgical dissection and decrease the engorged renal hilum [6].
- (ii) Surgical access and incisions [5].

Incisions were abdominal and thoracic. The original approaches were based on midline laparotomy or chevron (roof-top, bilateral Kocher) incisions affording only transdiaphragmatic access to the IVC and right atrium [10]. Later in the series, abdominal

incisions were combined with sternotomy or thoracotomy. This involved the cardiothoracic surgeon the preoperative planning.

(iii) Cavotomy and reconstruction of the IVC.

The perioperative management of the IVC is based on principles influenced by hepatic transplantation [6]: resection with curative intent, avoidance of narrowing the lumen, and control of the tumour thrombus. It is evident that the options are

- (a) cavotomy and direct closure, where 50% of the lumen can be preserved [6];
- (b) patch closure or resection with interposition graft.

Occasionally, the IVC lumen has been surgically obliterated, yet this option is rather dated and not routinely used. IVC Filters are used in circumstances of growth occluding the lumen and history of proximal emboli [6]. Sequential clamping of the IVC [8] may lead to hypotension, managed (in the absence of CPB) with preemptive Trendelenburg position and liberal volume expansion.

(iv) Surgical bleeding and transfusion requirements.

Extensive retroperitoneal dissection and cardiovascular sub procedures predispose to considerable bleeding, especially from engorged collateral phrenic veins. The management of intravascular volume is paramount to a favourable outcome (see also the previous paragraph on IVC clamping). It also accounts for the considerable perioperative transfusions [10].

- (v) Use of perfusion techniques.
- (vi) Mortality.
- (vii) Morbidity.
- (viii) Length of hospital stay.

3. Results and Analysis (Table 1)

29 series [2, 8, 10–36] with 784 patients from the last four decades offer cumulated perioperative data; 453 cases of ICTT-III and 331 of ICTT-IV were scrutinised. We included follow-up papers with the understanding that although their focus veered away from the perioperative period, their data for surgery were relevant to our review.

3.1. Demographics. Average age at operation was 59 years. 62% of the patients were male. 98% tumours were RCC. The remaining were Wilms', adrenal, and bladder tumours. 64% of primaries were in the right side, 36% on the left. There were no primary tumours from the anatomical midline. The laterality of tumour is relevant to operative planning as a left sided tumour presents a different pathological anatomy of the thrombus and the necessary intraabdominal dissection.

3.2. Imaging. It is paramount to determine the extent of the IVC growth in order to plan the bicoelomic access and dissection [6, 37]. 29% of patients had had preoperative tumour embolization via cavography as a measure to decrease the tumour burden and, importantly for the surgical team, reduce the expected blood loss by rending the culprit primary lesion and the organ (in 98% cases the kidney) relatively avascular. The contrast cavogram affords also a preoperative assessment of the extension of the thrombus.

3.3. Surgical Access and Incisions. The prevalent access was that of chevron (rooftop) incision with (27%) or without (34%) sternotomy.

37% of the patients were operated through the anatomical midline and 11% just by a median laparotomy.

3% of patients had some form of lateral thoracoabdominal incision. 86% of ICTT-IV had undergone sternotomy in combination with chevron (46%) or midline laparotomy (38%). The two teams operating on intracardiac extensions without opening the chest are also the "champions" of avoiding (albeit in small samples) CPB [10, 16].

The abdominal dissection has often been based on controlling of the porta hepatis (Pringle manoeuvre, with vascular loops under intermittent tension or soft vascular clamps) and the dissection of the liver known as "piggy-back" with minimal dissection of the IVC [10, 38].

- 3.4. Cavotomy and IVC Reconstruction. 12% of patients had resection of IVC and interposition graft. 55% of patients had a partial occlusion clamp on their preserved IVC, and 22% had cross-clamping of the preserved IVC.
- 3.5. Perfusion. 51% of total cases had no use of any perfusion technique (Table 1). We identified two extreme positions: nonuse in two small series [16, 25] and absolute indication [14, 20].

There was variability in most setups. Most surgeons retorted to invest in the (presumed expensive) perfusion techniques for ICTT-IV [11]; 88% of these intracardiac cases were operated with some form of bypass, reflecting the incidence of sternotomy in this subgroup. Moreover, circulatory arrest was used in 60% of ICTT-IV whilst in only 10% of ICTT-III. A small number of patients (5%) had only veno-venous bypass.

Average cardiopulmonary bypass time was 103 minutes (88 minutes for ICTT-III and 106 minutes for ICTT-IV). HCA times averaged 25 minutes (23 in ICTT-III and 26 in ICTT-IV).

- 3.6. Operating and Anaesthetic Times. The former average was 352 and the latter 362 minutes. The respective times for each subgroup were 339/331 minutes for ICTT-III and 378/396 minutes for ICTT-IV. We comment on these data.
- 3.7. Blood Loss and Transfusions. The magnitude of the operations can be appreciated by the considerable average blood loss and transfusion volumes: 2.6 L of blood loss and 2.4 L of blood products for ICTT-III and 3.7 L of blood loss and 3.5 L of blood products for ICTT-IV (Table 1).

3.8. Mortality. This was 10% (5% for ICTT-III and 15% for ICTT-IV).

3.9. Morbidity. Any-or-none morbidity was 56% (36% for ICTT-III, 64% for ICTT-IV). Most common complications were related either to perioperative bleeding (and reexploration) or thromboembolism (Table 1). Incidence of acute renal failure was 4%.

3.10. Length of Hospital Stay. That was 13 days. This is an important outcome measure that has to be weighed against variation of health policies and balance of tertiary to primary care worldwide.

4. Discussion

Multidisciplinary surgery for ICTT is a formidable undertaking that has elicited debate [38]. Resourcefulness [18] and collaboration are essential.

The authorship of the various series includes primarily noncardiothoracic surgeons [6]. The ample literature is skewed towards the urological/general surgical point of view, and our paper aspires to balance this.

4.1. Choice of Incision and the Cardiothoracic Surgeon. The contrast of opinion on choice of incision is germane to the involvement of the cardiothoracic surgeon in ICTT. Incisions vary between surgeons and relate to the extracardiac or intracardiac level of thrombus [22, 27, 30, 31, 33]. The debate is akin to that of en bloc or trans hiatal oesophagectomies. The abdominal approach has a lot in common with hepatic transplantation [10]. The risk of cardiac impaction of thrombus during such transdiaphragmatic procedures, especially during the manoeuvres of "milking" the IVC retrogradely [10], has in fact led to earlier involvement of cardiothoracic surgeons; a thoracic incision preempts the need for intracardiac disimpaction of tumour thrombus [39]. It is noted that the two teams reporting no CPB whatsoever have small total numbers and only four patients with ICTT-IV. It was expected that most surgeons would consider perfusion for all the ICTT-IV [11] and some ICTT-III [8], especially where preoperative imaging could not exclude intracardiac thrombus. It is evident that assessment of the cranial extent of the thrombus by preoperative imaging can be inaccurate [40–43]. It follows that preemptive involvement of the cardiothoracic specialists, including anaesthetists and perfusionists, is prudent, especially where they are not available on site.

The sternotomy offers the facile option of central cannulation for cardiopulmonary bypass with either of Ross basket, "two-stage," or bicaval cannulation depending on preference and extend of thrombus. The peripheral (femoral or axillary [9]) cannulation is of course available when there are concerns for the extent of thrombus around the possible IVC cannulation areas. Preemptive hypothermic circulatory arrest [13] necessitates sternotomy. CPB can, according to one well-presented school of thought [23], only be avoided with caution in the presence of a free-floating thrombus.

That is how the risk of intraoperative tumour embolization (that has being reported as cause of death [28, 30]) is managed efficiently. The Sloan-Kettering group had previously pursued a very well described transabdominal technique [16], possibly because of the limited access to inhouse cardiac surgery, yet they have changed recently.

We note that the HCA times were reasonable and no HCA-attributable incidents were recorded in any of the subjects. Of note also is the potential of HCA to create a "bloodless field" of dissection [8] and facilitate the intraatrial manoeuvring of the thrombus in relation to the outflow cannula.

4.2. Blood Conservation. We further note the need of massive transfusions (replacement of body blood volume in 24 hours or half of blood volume in 4 hours). Heparinisation for CPB, even after completing the abdominal dissection [38], would account for the 26% bleeding morbidity in ICTT-IV, where CPB was used in almost 9 out of 10 patients. On the other hand, the cost and implications could drive a reexpansion of the indications of aprotinin [44] or utilising tranexamic acid [45]. By the same token, cell saving techniques will be of relevance; some of the shed blood can be returned to the patient through the Intraoperative perfusion circuit or the cell saver apparatus. Procoagulant and blood conservation strategies, including biological and synthetic glues, may reduce the need for transfusion; the patients' intact immunocompetence is important in the primary diagnosis of malignancy. The presence of an anaesthetic team with experience in cardiovascular anaesthesia is essential [10].

4.3. Preoperative Embolisation. Stark contrasting on opinions is noted [46–48]. Its strong critics [47] proffer nonrandomised retrospective data of two groups with 30% difference in presence of ICTT. There is one propensity-matched study in favour of embolisation [48]. This technique also relates inversely to use of preemptive HCA. We note the emerging capabilities of diffusion weighted magnetic resonance, especially in accurate definition of the level and nature of the thrombotic lesions [49].

4.4. Morbidity and Mortality. Complications are to be expected in more than half of patients. We found that morbidity and mortality varied between lower and higher levels of tumour; intracardial extension rends surgery three times riskier, yet tumour extension has not always been found to affect long-term survival [32, 35, 50]. Acute renal failure and renal support appear as a relatively rare complication, given that 98% of patients had a nephrectomy and three out of ten had their left cancerous kidney removed.

The times recorded indicate long procedures (exceeding 5 hours in average) and also unveiling a weakness in recording operating and anaesthetic times; these appear similar instead of at least 30 minutes difference, affording time for anaesthetic induction and insertion of multiple monitoring lines [7].

5. Conclusions

Close multidisciplinary collaboration has led to acceptable operative risks for ICTT. We propose that it is achieved more efficiently in hospitals with on-site cardiothoracic teams. We consider the following advantages of such policy:

- (i) management of blood loss, with the expertise in preempting and correcting the circulatory events inevitable to such extensive cardiovascular procedures and haemostasis, with experience in all aspects of adjuncts (glues and other technologies [45]),
- (ii) risk management of fracture thrombi [39], with the advantage of preemptive extracorporeal perfusion.

A standard of care for ICTT is emerging. The cardiothoracic surgeon is increasingly involved [19, 37] were previously excluded from their management [10, 16, 51]. We believe that preemptive cardiothoracic consultation is instrumental in developing such standard of care. In the United Kingdom, the National Institute for Clinical Excellence has already mandated the preemptive referral to the cardiothoracic team for all ICTT in at least one region (to Wythenshawe Hospital, Manchester, UK). A streamlined procedure plan would be especially advantageous if technical performance was to be scored [52] in order to convince the stakeholders where the local setup is reluctant to change [16]; a marginal analysis [53] would recommend reallocating resources to increase efficiencies.

6. Limitations

Retrospective reviews have to be interpreted cautiously; limitations have been previously outlined in a small self-reporting multicentre review of ICTT-IV [16].

We further note that potential causes of bias are

- (i) reporting bias
- (ii) control for comorbidities, which influence mortality and unbalance any attempt to compare interventions,
- (iii) missing variables, especially in relation with the morbidity,
- (iv) nonuniform definition of complications between centres [23], and
- (v) lack of detailed perioperative patient information for series that focus on followup rather than the surgery itself.

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