Simplified perfusion strategy for removing retroperitoneal tumors with extensive cavoatrial involvement

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Objectives: Our objective was to compare effectiveness and safety of a simplified approach for removing retroperitoneal tumors with extensive cavoatrial involvement using beating-heart cardiopulmonary bypass (CPB) versus hypothermic circulatory arrest (HCA).

Methods: From January 1984 to January 2009, 144 patients underwent radical nephrectomy and inferior vena caval tumor thrombectomy, 56 (39%) using CPB and 88 (61%) HCA. Compared with HCA patients, CPB patients were of similar age (62 ± 10 vs 60 ± 11 years, $P = .4$) and gender (39% vs 39% female, $P > .9$), with similar stroke history (3.6% vs 2.3%, $P = .6$), but had less pulmonary disease (18% vs 33%, $P = .06$) and lower preoperative creatinine concentration (1.3 ± 0.72 vs 1.5 ± 0.86 mg $\cdot$ dL⁻¹, $P = .04$).

Results: Complete tumor removal was achieved in all patients by both strategies. Compared with HCA procedures, CPB times were shorter (50 ± 33 vs 94 ± 40 minutes, $P < .0001$). CPB patients required fewer blood transfusions (36% no transfusion vs 17%, and 45% ≥ 4 units vs 72%; $P = .003$) and had no statistical difference in morbidity, including reoperation for bleeding (3.8% vs 8.0%, $P = .3$), renal failure requiring dialysis (3.6% vs 10%, $P = .14$), respiratory insufficiency (21% vs 19%, $P = .8$), sepsis (5.4% vs 10%, $P = .3$), stroke (5.4% vs 1.1%, $P = .13$), and in-hospital mortality (7.1% vs 13%, $P = .3$). Ten-year survival (22% vs 22%, $P > .9$) and freedom from cancer recurrence (24% vs 28%, $P = .8$) were similar.

Conclusions: Radical nephrectomy and removal of inferior vena caval tumor–thrombus can be simply, effectively, and safely performed with beating-heart CPB, avoiding the deleterious effects of HCA and providing clinical benefit without increasing morbidity or mortality. (J Thorac Cardiovasc Surg 2012;143:1014-21)

Retroperitoneal tumors, especially renal cell carcinoma, tend to spread into the venous system, growing toward the inferior vena cava (IVC).¹ In advanced stages, they spread extensively into the suprahepatic IVC and right atrium (level III/IV),² initiating thrombus formation. Adjunct cardiopulmonary bypass (CPB) with hypothermic circulatory arrest (HCA) has been the standard technique for providing a virtually bloodless surgical field for successful tumor removal.³ However, it is associated with long perfusion time, coagulopathy with postoperative bleeding,

cardiopulmonary complications, and end-organ dysfunction, leading to substantial morbidity and mortality.^{1,3}

Beginning in the 1990s, we have explored a simplified alternative surgical and perfusion technique using beating-heart CPB without circulatory arrest (Figure 1). Purposes of this study were to (1) detail this alternative approach to treating retroperitoneal tumors with extensive cavoatrial involvement, (2) address its advantages and limitations, and (3) assess its effectiveness and safety compared with HCA.

PATIENTS AND METHODS

Patients

From January 1984 to January 2009, 144 patients at Cleveland Clinic had adjunct CPB for resection of primary retroperitoneal renal tumors with level III/IV tumor–thrombus extension. Of these, 56 (39%) underwent resection using CPB (CPB group) and 88 (61%) using HCA (HCA group). Age of the CPB group was similar to that of the HCA group (62 ± 10 vs 60 ± 11 years, $P = .4$), as was gender (39% vs 39% female, $P > .9$) and history of stroke (3.6% vs 2.3%, $P = .6$). However, CPB patients had lower preoperative serum creatinine levels (1.3 ± 0.72 vs 1.5 ± 0.86 mg $\cdot$ dL⁻¹, $P = .04$) and less chronic obstructive pulmonary disease (18% vs 33%, $P = .06$) (Table 1).

Preoperative demographic and comorbidity data and postoperative complications until time of patient discharge were obtained from the prospective Cardiovascular Information Registry, supplemented by medical record review. The Institutional Review Board of the Cleveland Clinic approved collecting and using these data for research, with patient consent waived.

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This study was supported in part by the Kenneth Gee and Paula Shaw, PhD, Chair in Heart Research (to Dr Blackstone). Gregory Pattakos, MD, MS, is a National Heart, Lung and Blood Institute Clinical Research Scholar of the Cardiothoracic Surgical Trials Network, and his master of science in clinical research has been funded by National Institutes of Health grant 1U01HL088955-01. No sponsor had direct involvement of any kind in this research study.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Sept 24, 2010; revisions received April 21, 2011; accepted for publication May 18, 2011; available ahead of print July 25, 2011.

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0022-5223/\$36.00

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doi:10.1016/j.jtcvs.2011.05.009

Abbreviations and Acronyms

- CPB = cardiopulmonary bypass
 HCA = hypothermic circulatory arrest
 IVC = inferior vena cava
 PFO = patent foramen ovale
 SVC = superior vena cava

Maximum cephalic intravascular tumor extent was classified according to guidelines developed by Neves and Zincke²: level I, in the IVC at the renal vein; level II, to the infrahepatic IVC; level III, to the retrohepatic IVC; and level IV, to the supradiaphragmatic IVC or right atrium. Tumor extent in all patients in our study was level III or IV.

Perfusion and Operative Techniques

Objectives.

1. Provide a bloodless surgical field for safe, complete removal of primary tumor and its IVC/right heart tumor–thrombus extension by:
 - Avoiding life-threatening pulmonary and systemic embolization of fragmented tumor–thrombus
 - Securing adequate vessel control (lumbar, adrenal, and suprahepatic veins) for reduction of blood loss and effective blood salvage
2. Resolve or palliate IVC obstruction symptoms
3. Improve survival

Preoperative assessment and indications. Imaging studies to assess extent of the primary tumor and cavoatrial involvement included chest radiography, computed tomography of the chest and abdomen, selective renal and vena caval angiography, cardiac catheterization, echocardiography, and magnetic resonance angiography. Since the advent of intraoperative transesophageal echocardiography, it has been routinely used to confirm intravascular tumor–thrombus location, identify occurrence of distal embolization, assess completeness of resection, diagnose a patent foramen ovale (PFO) or atrial septal defect, detect intracardiac air during CPB, and monitor cardiac performance.

The decision to use adjunct CPB was based on proximity of the vena caval tumor–thrombus to the major hepatic veins and the cephalic supradiaphragmatic extension of the tumor. In general, venous thrombi at or above the level of the major hepatic veins were referred for CPB.

Surgical preparation. Early in the experience, preoperative selective renal artery ethanol embolization was performed the day before surgery according to surgeon preference ($n = 60$), but this is no longer our practice.

We have previously described the surgical technique for renal cell and IVC tumor–thrombus removal with HCA.³ With either technique, operations are performed through 2 incisions: a transverse laparotomy (chevron incision) and a median sternotomy (Figure 2), without dividing the diaphragm. Pericardial and peritoneal cavities are approached separately, without connecting them. This approach provides adequate exposure, facilitates healing, and decreases potential for hypoperfusion and necrosis of the triple point where both incisions are connected. After exposure of the kidney and a variable length of the infrarenal and suprarenal IVC, nephrectomy is performed to allow better access to, and exposure of, the IVC at the level of the renal veins and retrohepatic segment. Local regional lymphadenectomy is performed when preoperative or intraoperative findings suggest lymph node involvement. Thereafter, the IVC is exposed for tumor thrombectomy, and meticulous hemostasis in the retroperitoneum is obtained before initiating CPB.

Perfusion strategies. Systemic heparinization (activated clotting time >500 seconds) is established by administering $300 \text{ IU} \cdot \text{kg}^{-1}$. Distal

FIGURE 1. Time trends of cardiopulmonary bypass (CPB) versus hypothermic circulatory arrest (HCA) for inferior vena cava tumor operations.

venous return is diverted by IVC cannulation (22F-24F) between bifurcation and renal veins, and proximal return is diverted by right atrial cannulation (24F-28F) directed toward the superior vena cava (SVC) or by direct SVC cannulation with a right-angled 24F cannula. The ascending aorta is cannulated with a 24F arterial cannula (Figure 3) with bicaval cannulation. The IVC cannulation site is inferior to the intra-abdominal tumor. These 2 cannulas drained most of the venous return from the upper and lower body, but additionally, 2 cardiectomy suckers were used to drain blood from the right atrium and opened IVC to optimize visualization. Blood was filtered through a $40\text{-}\mu\text{m}$ leukocyte reducing filter (LukoGuard LGB; Pall Corporation, East Hills, NY) interposed in the arterial line. A blood-salvage system was used to assist in maintaining a bloodless field as well as to conserve blood.

HCA strategy. CPB is established and the body cooled to 19°C while retrograde cardioplegic solution is administered. A steroid and barbiturate are administered and ice is packed around the head for even cooling of the brain, after which CPB is stopped and the blood volume is drained into a reservoir. HCA is maintained while tumor–thrombus is being removed from the atrium, proximal IVC, and abdominal IVC.

CPB strategy. CPB is initiated with mild systemic hypothermia (32°C – 34°C) and beating heart (no aortic clamp or cardioplegic cardiac arrest). So that a near-bloodless field can be obtained for a simultaneous abdominal IVC and right atrial approach, a carefully executed strategy for diverting systemic venous return from the operative area is necessary.

IVC flow must be diverted upstream of the renal veins and blood from tributaries in the operative area (open IVC) removed to provide adequate visualization for tumor removal. Blood from the right atrium will also enter the operative area unless diverted.

Venous and arterial cannulation is performed in similar fashion as for HCA. With transesophageal echocardiography for visual guidance and care taken not to dislodge the tumor, the SVC and infrarenal IVC blood flow is diverted through their respective venous cannulas, as is contralateral renal vein blood flow. Then simultaneous incisions are made in the right atrium and longitudinally in the anterolateral aspect of the IVC (Figure 3).

Hepatic venous return is cleared with the aid of a vacuum-assisted suction device placed in the retrohepatic IVC, and coronary sinus and upper body venous return are cleared by a similar device placed in the right atrium, achieving a clear operative field for complete tumor removal with minimal blood loss (Figure 3). Blood cleared in this fashion is processed through a blood-salvage system before being returned to the perfusion circuit.

TABLE 1. Patient characteristics according to perfusion strategy

Variable	n*	CPB (n = 56)		HCA (n = 88)		P
		no. (%)	n*	no. (%)		
<i>Demographics</i>						
Age (y), mean ± SD	56	62 ± 10	88	60 ± 11		.4
Female	56	22 (39)	88	34 (39)		>.9
<i>Cardiovascular comorbidity</i>						
Previous cardiac operation	51	4 (7.8)	39	5 (13)		.4
Previous MI	51	9 (18)	39	5 (13)		.6
Heart failure	51	4 (7.8)	39	4 (10)		.7
Atrial fibrillation/flutter	51	1 (2.0)	39	0 (0)		.4
Previous stroke	56	2 (3.6)	88	2 (2.3)		.6
Carotid disease	51	6 (12)	39	1 (2.6)		.11
Peripheral arterial disease	51	7 (14)	39	2 (5.1)		.18
Hypertension	50	30 (60)	38	24 (63)		.8
<i>Noncardiac comorbidity</i>						
Chronic renal disease	56	4 (7.1)	88	14 (16)		.12
Smoking	49	31 (63)	36	20 (56)		.5
COPD	45	8 (18)	75	25 (33)		.06
Diabetes mellitus	51	7 (14)	39	10 (26)		.15
<i>Cancer</i>						
Histopathologic cell type	56		88			
Renal		53 (95)		82 (93)		.7
Adrenocortical carcinoma		2 (3.6)		1 (1.1)		.6
Sarcoma		1 (1.8)		2 (2.3)		>.9
Primitive neuroectodermaltumor		0 (0)		1 (1.1)		>.9
Malignant fibroushistiocytoma		0 (0)		1 (1.1)		>.9
Pheochromocytoma		0 (0)		1 (1.1)		>.9
<i>Pathologic classification</i>						
pT	56		85			
2b		1 (1.8)		2 (2.4)		.8
3b		11 (20)		8 (9.4)		.08
3c		39 (70)		70 (82)		.08
4		5 (8.9)		5 (5.9)		.5
pN1	56	10 (18)	84	11 (13)		.4
pM1	56	15 (27)	85	18 (21)		.4
Tumor size (cm), mean ± SD	54	9.4 ± 3.9	75	10 ± 4.6		.7

CPB, Cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SD, standard deviation; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease.

*Patients with data available.

Tumor removal. Through an oblique right atrial incision, the interior of the right atrium, tricuspid valve and subvalvular apparatus, and proximal IVC are explored, and controlled mobilization and removal of tumor–thrombus is performed under direct visualization. The tumor is carefully peeled away from the right atrial wall and IVC simultaneously and removed en bloc through the cavotomy. In case of dense adherence, an end-arterectomy spatula is used to peel the thrombus off the IVC endothelium. The vena cavotomy and tumor-filled renal vein ostium are excised with the tumor–thrombus. In the setting of adherent tumor–thrombus or invasion into the IVC wall, the IVC wall is also resected with the tumor–thrombus. In cases of tumor–thrombus extension into the pulmonary artery, an access incision is made in the pulmonary trunk proximal to its bifurcation.

Intraoperative assessment of complete tumor resection is performed under direct visualization of the right atrial wall as well as the intrahepatic and infrahepatic IVC, and by advancing a balloon or Foley catheter from the abdominal IVC to the right atrium, or performing an index finger maneuver, to confirm a clean resection.

Because of IVC dilatation, its remnant lumen after removal of the tumor is of normal diameter in most patients, permitting cavotomy closure with a running 4-0 monofilament polypropylene suture technique without

narrowing the lumen. If more than half the IVC circumference is resected, satisfactory IVC size can be achieved by patch reconstruction with autologous or bovine pericardium, or polytetrafluoroethylene (PTFE; W. L. Gore and Associates, Inc, Flagstaff, Ariz).

Concomitant procedures. In the event a PFO or atrial septal defect is present or the tumor extends into the right ventricle, or if there is need to perform concomitant cardiac procedures, the heart is arrested with cold blood cardioplegic solution (4°C) for tumor removal and surgical correction of associated cardiac disease. Those patients with pulmonary tumor embolus usually require HCA to remove emboli from the pulmonary artery branches.

After closure of vascular and cardiac incisions, patients are rewarmed and weaned from CPB. Anticoagulation is reversed by protamine administration, and after satisfactory hemostasis is achieved, incisions are closed in standard fashion.

Data Analysis

Categorical variables were compared using Fisher's exact or χ^2 tests, as appropriate, and continuous variables were compared using the Wilcoxon

FIGURE 2. Surgical exposure. Adequate exposure of retroperitoneal tumor and caval tumor–thrombus requires a median sternotomy to expose the right atrium (A) and a transverse laparotomy (chevron incision) with mobilization of the parietocolic fascia to access the retroperitoneal tumor and inferior vena cava (B).

rank sum test. Time-related events were analyzed nonparametrically by the Kaplan-Meier method and parametrically by a multiphase hazard model.⁴

Follow-up. Systematic cross-sectional follow-up was performed in January and February 2011 to assess cancer recurrence and vital status. Among patients in the HCA group, 12 were lost to follow-up. Median follow-up time was 0.77 year; 25% still at risk of recurrence were followed up more than 22 years and 10% more than 24 years. Among patients in the CPB group, 9 were lost to follow-up. Median follow-up was 0.83 year; 25% still at risk of recurrence were followed up more than 13 years and 10% more than 14 years. For patients with metastatic (pM1) disease at resection, recurrence was defined as a new site of metastasis.

The Social Security Master Death File was used to supplement this cross-sectional follow-up for vital status.^{5,6} Median follow-up was 1.3 years; 25% were still alive more than 14 years and 10% more than 22 years after operation.

Data Presentation

Continuous variables are summarized by mean $\pm$ standard deviation or by median and 15th and 85th percentiles, consistent with ± 1 standard deviation. Categorical data are summarized by frequencies and percentages. All analyses were performed using SAS (SAS, Inc., Cary, NC) statistical software (version 9.1).

RESULTS

Effectiveness

Complete tumor resection was achieved in all patients by both surgical strategies.

Safety

Patients in the CPB group had shorter CPB times (50 ± 33 vs 94 ± 40 minutes, $P < .0001$) and no HCA time versus 22 ± 11 minutes in the HCA group. Both groups had similar

myocardial ischemic times (15th, 50th, and 85th percentiles, 0/12/54 versus 19/32/52 minutes; $P = .2$). Myocardial arrest was not necessary for tumor removal in the CPB group; it was used for concomitant coronary artery bypass grafting in 7 (13%) patients versus 1 (1.0%) in the HCA group, and for PFO closure in 3 (1 before tumor removal), accounting for similarity of myocardial ischemic times.

CPB patients received fewer blood transfusions than HCA patients (no red blood cells in 36% vs 17%, $P = .003$) (Table 2). Although postoperative complications were fewer in CPB patients (27% vs 34%, $P = .4$), with lower occurrence of renal failure requiring dialysis (3.6% vs 18%, $P = .14$) and hospital mortality (7.1% vs 13%, $P = .3$), these findings could be due to chance. From 2002 to 2009, hospital mortality for patients in the CPB group was 3.4% (1/29 patients; 68% confidence limits 0.7%-11%).

CPB patients experienced more perioperative strokes (5.4% vs 1.1%, $P = .13$), but this, too, could be due to chance (Table 3). PFO was present in all 3 cases, undiagnosed preoperatively. Two were discovered by transesophageal echocardiography after discontinuing CPB and were associated with left ventricular air. Although the PFOs were closed, the patients had watershed infarcts on postoperative computed tomography. In the third patient, the PFO was identified before CPB, the heart arrested, and the PFO closed. Nevertheless, a small lacunar infarct of uncertain age was detected by magnetic resonance imaging, and the transient defect completely resolved before discharge.

FIGURE 3. Perfusion technique. Both perfusion strategies use the same cannulation procedures: 2 venous cannulas (A) and 1 aortic cannula and arterial filter (B). For beating-heart cardiopulmonary bypass, 2 additional pump suckers (C) are used to create a bloodless surgical field. A blood-salvage system (D) is also used for blood conservation.

Length of intensive care unit stay was similar between groups (median 3 days in both groups, $P = .6$), as was post-operative length of stay (8.5 days in the CPB group vs 10 days in the HCA group, $P = .2$).

Of patients in the CPB group, 30 had at least 1 recognized cancer recurrence, and in the HCA group, 46 experienced a recurrence. In both groups, distant metastases predominated, with recurrence in the liver more frequent in the HCA group (33% vs 10% of those with recurrences, $P = .03$) and recurrence in bone more common in the CPB group (43% vs 13% of those with recurrences, $P = .003$) (Table 4). Recurrence at multiple sites was more common in the CPB group (50% vs 24% of those with recurrences, $P = .02$). However, overall freedom from cancer recurrence was similar between groups: 57%, 30%, 24%, and 20% in the CPB group versus 55%, 31%, 28%, and 27% in the HCA group ($P[\log\text{-rank}] = .7$) at 1, 5, 10, and 15 years, respectively (Figure 4). Survival after operation was also similar: 58%, 33%, 22%, and 17% in the CPB group versus 57%, 32%, 22%, and 17% in the HCA group ($P[\log\text{-rank}] > .9$) at 1, 5, 10, and 15 years, respectively (Figure 5).

DISCUSSION

We have described a simplified approach to perfusion support for complete removal of tumor-thrombus involving the IVC that employs beating-heart CPB. Effectiveness of complete tumor-thrombus removal was comparable with that for HCA, with decreased transfusion needs and a similar safety profile.

Perfusion Strategies

Some reports with a limited number of patients have advocated using continuous beating-heart CPB to avoid HCA for complete removal of retroperitoneal tumors with extensive cavoatrial involvement.^{7,8} We moved progressively over the past 2 decades from HCA to continuous CPB, which provides adequate exposure and a near-bloodless field for the surgeon while avoiding complexity and risks of HCA. Although femoral vein cannulation can adequately drain the lower body, we do not use this technique because it requires an additional incision, with potential associated complications including lymphocele, infection, and compartment syndrome, which could compromise postoperative recovery.

TABLE 2. Blood product use

Blood product	CPB (n = 56)		HCA (n = 88)	
	n*	No. (%)	n*	No. (%)
RBC units	56		87	
0		20 (36)		15 (17)
1		3 (5.4)		3 (3.4)
2		7 (13)		2 (2.3)
3		1 (1.8)		4 (4.6)
≥4		25 (45)		63 (72)
Any FFP plasma	56	18 (32)	83	48 (58)
Any platelets	56	15 (27)	82	48 (59)

CPB, Cardiopulmonary bypass; HCA, hypothermic circulatory arrest; RBC, red blood cell; FFP, fresh frozen plasma. *Patients with data available.

TABLE 3. Postoperative complications

Complication	CPB (n = 56)	HCA (n = 88)	P
	no. (%)	no. (%)	
Hospital mortality	4 (7.1)	11 (13)	.3
Reoperation for bleeding	2 (3.6)	7 (8.0)	.3
Renal failure requiring dialysis	2 (3.6)	9 (10)	.14
Respiratory insufficiency	12 (21)	17 (19)	.8
Stroke	3 (5.4)	1 (1.1)	.13
Myocardial infarction	0 (0)	1 (1.1)	.4
Sepsis	3 (5.4)	9 (10)	.3
Any complication	15 (27)	30 (34)	.4

CPB, Cardiopulmonary bypass; HCA, hypothermic circulatory arrest.

Effectiveness

Regardless of perfusion technique used, complete surgical resection of level III/IV tumor–thrombus requires 2 multidisciplinary teams to perform a major operation with complete exposure and dissection in the abdomen and thorax.⁷⁻⁹

For patients with more limited IVC tumor extension, recent publications have described surgical approaches to avoid sternotomy and CPB.¹⁰⁻¹³ Some of these involve temporary occlusion of the proximal IVC with a balloon, venovenous bypass and limited anticoagulation, or IVC staple ligation and en bloc resection of level III tumor–thrombus occluding the IVC in patients who have adequate collaterals and no edema in the lower limbs. Although these strategies are reported to have good results for level II/III tumors, they would not be considered for patients with level IV cavoatrial extension, for which a more extensive resection is necessary. Direct vision, which we advocate, decreases risk of distal embolization that may result when mobilization is done by blind dissection.

Safety

Outcomes. Our study covers a period of 25 years during which evolution of anesthetic techniques, surgical techniques, and postoperative care led to improved operative results. This must be kept in mind when interpreting our overall hospital mortality of 7.5% and 13%; more recent series of level III/IV tumor resection report mortalities between 3% and 10%.^{14,15} Other authors have reported mortality of up to 40% if the IVC tumor extended above the diaphragm in the IVC.^{16,17}

The HCA group had longer CPB times, primarily owing to the time required to cool and later rewarm the patient, although a more complex resection may have also contributed to these findings. In addition, these patients had a mean HCA time of 22 ± 11 minutes, during which end-organ vital function can be preserved only by decreasing systemic metabolic requirements.

CPB is associated with transient platelet dysfunction,¹⁸ and HCA may increase this effect and further affect coagulation.¹⁹ Not surprisingly, patients in the HCA group were

TABLE 4. Sites of recurrent cancer

Recurrence site*	CPB (n = 30†)	HCA (n = 46†)	P
	no. (%)	no. (%)	
Local	13 (43)	12 (26)	.12
Lymphatic	4 (13)	6 (13)	>.9
Regional	1 (3.3)	0 (0)	.2
Distant	3 (10)	6 (13)	.8
Lung	8 (27)	12 (26)	>.9
Liver	3 (10)	15 (33)	.03
Brain	6 (20)	5 (11)	.3
Bone	13 (43)	6 (13)	.003
Skin	1 (3.3)	2 (4.3)	.8
Multiple recurrence sites	15 (50)	11 (24)	.02

CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest. *Because of multiple recurrence sites, percentages add to more than 100%. †Patients who had a recurrence.

more likely to undergo reoperation for bleeding and required more blood product transfusions than patients in the CPB group, as others have reported.²⁰ Mounting evidence points to deleterious effects of allogeneic transfusion that have been associated with both tumor recurrence^{21,22} and postoperative infection.^{23,24}

The most frequent postoperative complication in both groups was respiratory insufficiency, likely owing to the extent of median laparotomy and sternotomy incisions. Thus, pain control and adequate respiratory therapy with incentive spirometry are essential in postoperative management.

We observed less renal dysfunction and sepsis in the CPB group. Only 1 patient in our entire series experienced a perioperative myocardial infarction (HCA group), comparing favorably with previous reports²⁵; this is probably related to thorough preoperative cardiac assessment in all patients, with coronary catheterization performed preoperatively when indicated.

Stroke in the early CPB experience was associated with a PFO in all 3 cases. We recommend preoperative and intraoperative imaging for PFO diagnosis. If it is present, the heart should be arrested and the PFO closed before commencing tumor removal.

The only concomitant cardiac operation was coronary artery bypass grafting in 8 patients. This did not increase postoperative complications or mortality.

Postoperative length of stay was similar in both groups, comparing favorably with earlier reports that describe longer hospital stays even in patients not undergoing HCA.²⁶

Cancer spread during CPB. CPB requires reinfusion of salvaged blood, possibly increasing the chances of tumor metastasis more than with HCA. Although a higher proportion of patients in the CPB group had multiple recurrence sites, overall likelihoods of cancer recurrence and survival were similar to those of the HCA group. Gray and colleagues²⁷ studied biomarker cancer recurrence in patients undergoing radical retropubic prostatectomy with intraoperative cell salvage and autotransfusion using a leukocyte

FIGURE 4. Freedom from cancer recurrence after operation stratified by perfusion strategy. Each symbol represents a death, vertical lines 68% confidence limits, and numbers in parentheses patients remaining at risk. Solid line is parametric estimate enclosed within 68% confidence bands. For pM1 patients, recurrence was defined as a new site of metastasis. CPB, Resection using continuous cardiopulmonary bypass and a beating heart; HCA, resection using hypothermic circulatory arrest.

reduction filter as the sole blood management technique. They compared this with that of patients who predonated 1 to 3 units of autologous blood. Cell salvage did not appear to be associated with an increased risk of early biochemical progression. Nieder and colleagues²⁸ reported that routine use of cell-salvaged blood did not adversely affect midterm

survival (3-year follow-up) of 378 patients undergoing radical cystectomy.

Catling and colleagues²⁹ found that patients undergoing surgery for gynecologic cancers demonstrated circulating cells at the time of removal, and in more than half, cancer cells were present in blood aspirated with a cell-salvage

FIGURE 5. Survival after operation stratified by perfusion strategy. Format is as in Figure 4. CPB, Resection using continuous cardiopulmonary bypass and a beating heart; HCA, resection using hypothermic circulatory arrest.

system. A leukodepleting filter effectively removed these cells in all cases. We have used an intraoperative blood-salvage system since 2000 in both CPB and HCA patients, in keeping with current guidelines for urologic cancers.²⁷⁻²⁹

Blood is suctioned from the operative field and through a leukocyte depletion filter (LeukoGuard LGB) in the arterial line before it is returned to the patient.

LIMITATIONS

This single-institution observational clinical study spanned 25 years, so evolving approaches to surgical management and postoperative patient care may have confounded the results. Although we have compiled extensive data on each patient with respect to his or her cancer, we have limited the presentation of these data to major pathologic characterization and to cancer recurrence and survival. In addition, HCA was used only for more difficult cases in more recent times, which may have biased our results in favor of CPB.

CONCLUSIONS

Radical removal of retroperitoneal tumors with extensive cavoatrial involvement can be simply, effectively, and safely performed with beating-heart CPB, avoiding the deleterious effects of HCA. Performing additional cardiac procedures does not adversely affect operative outcomes.

We thank the late Andrew C. Novick, MD, for initiating the study of these patients, compiling characteristics of the cancer, and following many of them. We also thank Jiansheng Zhong, MA, for data management, and Tess Parry, BS, for editorial assistance.

References

1. Marshall VF, Middleton RG, Holswade GR, Goldsmith EI. Surgery for renal cell carcinoma in the vena cava. *J Urol*. 1970;103:414-20.
2. Neves RJ, Zincke H. Surgical treatment of renal cancer with vena cava extension. *Br J Urol*. 1987;59:390-5.
3. Novick AC, Kaye MC, Cosgrove DM, Angermeier K, Pontes JE, Montie JE, et al. Experience with cardiopulmonary bypass and deep hypothermic circulatory arrest in the management of retroperitoneal tumors with large vena caval thrombi. *Ann Surg*. 1990;212:472-6; discussion 476-7.
4. Blackstone EH, Naftel DC, Turner ME Jr. The decomposition of time-varying hazard into phases, each incorporating a separate stream of concomitant information. *J Am Stat Assoc*. 1986;81:615-24.
5. Boyle CA, Decoufle P. National sources of vital status information: extent of coverage and possible selectivity in reporting. *Am J Epidemiol*. 1990;131:160-8.
6. Newman TB, Brown AN. Use of commercial record linkage software and vital statistics to identify patient deaths. *J Am Med Inform Assoc*. 1997;4:233-7.
7. Skinner DG, Pritchett TR, Lieskovsky G, Boyd SD, Stiles QR. Vena caval involvement by renal cell carcinoma. Surgical resection provides meaningful long-term survival. *Ann Surg*. 1989;210:387-92; discussion 392-4.
8. Wagner B, Patard JJ, Mejean A, Bensalah K, Verhoest G, Zigeuner R, et al. Prognostic value of renal vein and inferior vena cava involvement in renal cell carcinoma. *Eur Urol*. 2009;55:452-9.
9. Vaidya A, Ciano G, Soloway M. Surgical techniques for treating a renal neoplasm invading the inferior vena cava. *J Urol*. 2003;169:435-44.
10. Rigberg DA, Jimenez JC, Lawrence PF. Balloon control of the suprahepatic inferior vena cava: a novel technique for renal cell carcinoma tumor thrombus. *Ann Vasc Surg*. 2008;22:200-2.
11. Yang Y, Sun S, Xiao X, Song Y, Cai W, Wang M, et al. Temporary balloon occlusion of inferior vena cava in resection of renal tumor with vena cava thrombus extension. *Urology*. 2009;73:645-8.
12. Granberg CF, Boorjian SA, Schaff HV, Orszulak TA, Leibovich BC, Lohse CM, et al. Surgical management, complications, and outcome of radical nephrectomy with inferior vena cava tumor thrombectomy facilitated by vascular bypass. *Urology*. 2008;72:148-52.
13. Shirodkar SP, Ciano G, Soloway MS. Vascular stapling of the inferior vena cava: further refinement of techniques for the excision of extensive renal cell carcinoma with unresectable vena-caval involvement. *Urology*. 2009;74:846-50.
14. Blute ML, Leibovich BC, Lohse CM, Cheville JC, Zincke H. The Mayo Clinic experience with surgical management, complications and outcome for patients with renal cell carcinoma and venous tumour thrombus. *BJU Int*. 2004;94:33-41.
15. Moizadeh A, Libertino JA. Prognostic significance of tumor thrombus level in patients with renal cell carcinoma and venous tumor thrombus extension. Is all T3b the same? *J Urol*. 2004;171:598-601.
16. Cherrie RJ, Goldman DG, Lindner A, deKernion JB. Prognostic implications of vena caval extension of renal cell carcinoma. *J Urol*. 1982;128:910-2.
17. Staehler G, Brkovic D. The role of radical surgery for renal cell carcinoma with extension into the vena cava. *J Urol*. 2000;163:1671-5.
18. Harker LA. Bleeding after cardiopulmonary bypass. *N Engl J Med*. 1986;314:1446-8.
19. Valeri CR, Feingold H, Cassidy G, Ragno G, Khuri S, Altschule MD. Hypothermia-induced reversible platelet dysfunction. *Ann Surg*. 1987;205:175-81.
20. Svensson LG, Crawford ES, Hess KR, Coselli JS, Raskin S, Shenaq SA, et al. Deep hypothermia with circulatory arrest: determinants of stroke and early mortality in 656 patients. *J Thorac Cardiovasc Surg*. 1993;106:19-28; discussion 31.
21. Woolley AL, Hogikyan ND, Gates GA, Haughey BH, Schechtman KB, Goldenberg JL. Effect of blood transfusion on recurrence of head and neck carcinoma. Retrospective review and meta-analysis. *Ann Otol Rhinol Laryngol*. 1992;101:724-30.
22. Jones KR, Weissler MC. Blood transfusion and other risk factors for recurrence of cancer of the head and neck. *Arch Otolaryngol Head Neck Surg*. 1990;116:304-9.
23. Kinoshita Y, Udagawa H, Tsutsumi K, Ueno M, Nakamura T, Akiyama H, et al. Usefulness of autologous blood transfusion for avoiding allogeneic transfusion and infectious complications after esophageal cancer resection. *Surgery*. 2000;127:185-92.
24. Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. *J Am Coll Surg*. 2006;202:131-8.
25. Al Otaibi M, Abou Youssef T, Alkhaldi A, Sircar K, Kassouf W, Aprikian A, et al. Renal cell carcinoma with inferior vena caval extension: impact of tumour extent on surgical outcome. *BJU Int*. 2009;104:1467-70.
26. Modine T, Haulon S, Zini L, Fayad G, Destrieux-Garnier L, Azzaoui R, et al. Surgical treatment of renal cell carcinoma with right atrial thrombus: early experience and description of a simplified technique. *Int J Surg*. 2007;5:305-10.
27. Gray CL, Amling CL, Polston GR, Powell CR, Kane CJ. Intraoperative cell salvage in radical retropubic prostatectomy. *Urology*. 2001;58:740-5.
28. Nieder AM, Manoharan M, Yang Y, Soloway MS. Intraoperative cell salvage during radical cystectomy does not affect long-term survival. *Urology*. 2007;69:881-4.
29. Catling S, Williams S, Freitas O, Rees M, Davies C, Hopkins L. Use of a leukocyte filter to remove tumour cells from intra-operative cell salvage blood. *Anaesthesia*. 2008;63:1332-8.