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Introduction

Despite transluminal tumor propogation into the inferior vena cava (IVC), radical nephrectomy with tumor thrombectomy in patients with renal cell carcinoma and level I to III thrombus extension is associated with a cancer-specific 5-year survival rate between 47% and 68%[1-6]. Renal cell carcinoma carries a special tropism for vascular involvement. Transluminal tumor propagation into the inferior vena cava occurs in 4% to 10% of patients undergoing surgery for renal cell carcinoma, and 14% to 39% of these patients exhibit level IV thrombus extension, i.e., suprahepatic extension to the right-sided cardiac chambers[2-7].

Although tumor thrombectomy of infradiaphragmatic tumor are relatively straight forward, supradiaphragmatic extension presents more technical challenges and mandates an individualized management protocol. Techniques of tumor thrombectomy in patients with renal cell carcinoma and level IV thrombus extension have evolved during the years[1-7]. Published literature documents a number of techniques with and without using cardiopulmonary bypass, hypothermia and exsanguinations[1-12]. However, most of these methods are plagued with problems like massive intraoperative bleeding, profound hypotension, suboptimal thrombectomy, tumor embolization, ischemic injury to vital organs, and perioperative mortality[1-12].

The non-cardiopulmonary bypass approaches include the following: a) the use of a finger to push back the tumor thrombus under a tourniquet around the intrapericardial inferior vena cava[6]; b) use of Foley catheter[13]; c) use of forceps[6,13]; d) use of Fogarty catheter[14]; e) mobilization with or without resection of the caudate lobe of the liver[15]; f) right posterolateral thoracoabdominal incision with a transdiaphragmatic approach for control of intrapericardial inferior vena cava[15]; g) bilateral subcostal incision with superior midline T-extension[16]; h) modified Chevron abdominal incision and a transdiaphragmatic approach; and i) veno-venous or vena caval-atrial bypass[8-10]. In isolated cases with extension of tumor thrombus till the level of inferior vena cava-right atrial junction, the thrombi is milked inferior to inferior vena cava-right atrial junction

and extracted like level III thrombi[8-12]. The advantages of these veno-venous or vena caval-atrial bypass with an electromagnetic centrifugal pump and vacuum-assisted drainage is avoidance of full heparnization and perioperative blood loss[8-12].

However, the non-CPB approaches in these clinical scenarios are fraught with problems of profound intraoperative hypotension, suboptimal thrombectomy, risk of tumor embolization within the right-sided cardiac chambers and pulmonary arterial tree, disruption of the inferior vena cava, massive intraoperative bleeding, and warm ischemic injury to the liver and kidneys[19,20]. Several reports of massive intraoperative pulmonary embolism requiring emergency pulmonary embolectomy have been published[19,20].

An attempt has been made to determine whether an organ transplant-based approach reduces the postoperative complications following radical nephrectomy and tumor thrombectomy in renal cell carcinoma with level II-IV thrombi. Although, a statistically significant reduction of operative morbidity was observed using transplant-based approach, all transplant-based patients were treated by a single, experienced, high volume surgeon from one centre (non-transplant-based patients were treated by various surgeons at 13 other centres) [21].

In an attempt to decrease or eliminate these dreaded complications in patients with renal cell carcinoma and level IV tumor extension, Marshall and associates in 1970 introduced the technique of tumor thrombectomy under cardiopulmonary bypass and hypothermia[13]. Hypothermia, cardiac arrest, and temporary exsanguinations with cardiopulmonary bypass facilitates controlled dissection, provides a bloodless field, and reduces the risk of tumor embolization[19,20]. However, up to 40% risk of complications including hepatic failure, renal failure, consumptive coagulopathy, postoperative sepsis and 33% perioperative mortality after hypothermic circulatory arrest have been reported by various investigators[5-7,19,20].

Different operative approaches for optimal surgical exposure have been described in the literature, namely, a midline, a thoracoabdominal, and a bilateral subcostal with superior midline T-extension[1-12,15-17].

In 2001, the corresponding author developed a technique of tumor thromectomy for renal cell carcinoma with level IV thrombus extension just above the inferior vena cava-right atrial junction on 2 patients through a posterolateral thoracoabdominal incision and transdiaphragmatic approach[15].

In 2007, the corresponding author developed a novel approach of radical nephrectomy and tumor thrombectomy in patients with level IV thrombus extension within the right-sided cardiac chambers by employing cardiopulmonary bypass, mild hypothermia, and intermittent supraceliac abdominal aortic occlusion, thus avoiding potential hematologic, hepatic, renal, neurologic and septic complications associated with circulatory arrest[22].

In our experience on six patients with level IV thrombus extension undergoing radical nephrectomy and tumor thrombectomy under cardiopulmonary bypass, mild hypothermia and intermittent supraceliac abdominal aortic occlusion, there were no early or late death. The ACCT was 12 and 15 minutes for two patients. The cumulative hepatic and renal ischemic times was 16 min and ranged from 14 to 22 minutes at ^{32}°C. The mean intraoperative blood loss was 492±73.6 ml (range 400-600ml). At the time of reporting, at a mean follow-up of 43±24.6 months (range 10 to 70 months) all patients remained disease free[22].

Ciancio et al in 2010 published their results on 102 patients undergoing resection of renal tumors extending into inferior vena cava through a modified chevron abdominal incision and a transdiaphragmatic approach. The tumor thrombus in 12 (13%) patients aged 12-80 years (median 63 years) extended into supradiaphragmatic inferior vena cava and right atrium. Four patients with level IV tumor invasion required sternotomy and removal under cardiopulmonary bypass and were excluded from their series. Mean operating time was 8 hours 15 minutes. Estimated blood loss was 2960 ml (range 500 to 7000 ml).

Several investigators at select institutions have reported successful application of robotic nephrectomy with inferior vena caval thrombectomy. Robotic management of level III tumor thrombi above the short hepatic veins have been performed reproducibly in select centres[23-27]. In these cases, the short hepatic veins are ligated, the right adrenal vein is controlled and the infrahepatic portion of inferior vena cava below the main hepatic veins in mobilized for cross-clamping. Level III Robot-assisted inferior vena caval thrombectomy (RA-IVCT) requires liver mobilization and clamping of first porta hepatis, and supra hepatic and infradiaphramatic inferior vena cava[23-27].

Two cadaver studies evaluating robotic access and isolation of the suprahepatic, infradiaphragmatic inferior vena cava have attempted to standardize the techniques for human application[28,29]. Investigators have developed thoracoscopic-assisted management of level IV thrombus under cardiopulmonary bypass[30-32]. Literature documents additional techniques for robotic RNIT including grafting of the inferior vena cava in cases with caval wall invasion, balloon occlusion of the vena cava and venacavoscopy to assess the lumen[33-34].

In 2019, Wang Q et al from Beijing, China reported the technique and results of 6 cases of level IV RA-IVCT under modified cardiopulmonary bypass. Thoracoscopy-assisted partial thrombectomy was performed for the intra-atrium

under cardiopulmonary bypass. Infradiaphragmatic RA-IVCT was completed in a manner similar to that of level III RA-IVR. In level IV cases where collateral circulation were reconstructed well, the "cavectomy, including thrombus" technique was used. The tumor inferior vena cava was enbloc resected[26].

One patient with level IV thrombus died on the first postoperative day due to extensive blood loss (12000 ml) and coagulopathy. Five patients had postoperative liver dysfunction and three had renal dysfunction. Median intraoperative blood loss was 2800 ml (range 1500-6000 ml). Three out of 6 (50%) patients had grade IV complications. Cardiopulmonary bypass time was 72 minutes (range 51-87 minutes) [26].

Preoperative identification of tumor thrombus infiltration of the inferior vena cava is indeed difficult. Various investigative modalities namely, intraoperative ultrasound and/or contrast enhanced ultrasound and preoperative magnetic resonance imaging have been used with unpredictable results[23-29]. These authors concluded that in cases of diffuse infiltration, robotic approach was excluded. The "cavectomy including thrombus" technique required caval replacement and these authors recommended open surgery in these cases[26].

Currently, no randomized studies or case-matched studies of open versus robotic surgery have been performed to allow more definitive conclusions regarding the superiority of one over the other. With our current knowledge, surgery for level III-IV RA-IVCR has proved to be highly risky and requires advanced robotic technique. Feasibility and reproducibility needs to be confirmed by other robotic surgeons. The procedure requires repositioning and redocking two to three times which is time consuming. Robotic inferior vena caval thrombectomy remains a highly challenging procedure and may only be appropriate for well selected patients and highly experienced surgeons[25,29]. Additionally, none of the robotic surgeons have employed clamping of the pulmonary artery to prevent tumor embolization during tumor thrombectomy from within the right atrium and right ventricle[22].

We describe here-in a male patient aged 56 years, diagnosed with right-sided renal cell carcinoma with level IV inferior vena caval tumor extension undergoing radical nephrectomy, and tumor thrombectomy under cardiopulmonary bypass, mild hypothermia, and intermittent supraceliac abdominal aortic occlusion. Postoperative recovery was uneventful.

Surgical Techniques

Patient position

The patient was placed in the supine position, with both groins exposed.

Intraoperative transesophageal echocardiography

Intraoperative transesophageal echocardiography was performed using a Hewlett-Packard Sonos 5500 ultrasound system (Hewlett-Packard Co, Andover, MA) to assess the cephalad extent of caval thrombus and adherence of the same, if any. Initially, the patient underwent exploratory midline celiotomy, and resectability was determined, limiting dissection around the IVC as much as possible. There was no evidence of metastatic disease.

Surgical approach

Laparotomy was performed using a midline abdominal incision. The liver, the omentum and the peritoneal cavity were inspected for any secondary tumor deposits. The laparotomy incision was extended cephalad with a median sternotomy. The pericardium was opened in between stay sutures using scissors, and not cautery to avoid inadvertent cautery-induced ventricular fibrillation on a distended, poorly contractile cardiac chambers.

Assessment of the extent of tumor

The cephalad extent of the tumor thrombus was palpated in the inferior vena cava and continued to extend within the right atrium, about 1 cm above the inferior vena cava-right atrial junction.

Exposure and cannulation of the femoral vein, ascending aorta and superior vena cava

An infrainguinal vertical incision was made over the femoral artery. The right femoral vein was dissected and looped to facilitate later cannulation. The ascending aorta, superior vena cava and right femoral vein were cannulated. For superior vena cava, an angled metal tipped venous cannula and for femoral vein, a long venous cannula (Edwards Lifesciences, LLC, One Edwards Way, Irvine, CA, USA) were used following systemic heparinization.

Control above the cranial extreme of the thrombus

The most important step at this stage is to gain control above the cranial extreme of the thrombus by placing a tourniquet or a Satinsky clamp, and all manipulations to the tumor-bearing organs were kept to a minimum until proximal control was obtained to avoid tumor embolization. It was possible to isolate and control the cavoatrial junction above the tumor using umbilical tapes. The main pulmonary artery in addition was dissected and looped to protect from a life-threatening pulmonary tumor embolization during assessment, palpation and mobilization of the tumor bearing organs.

Dissection of the right kidney and retroperitoneal great vessels

During dissection of the right kidney, the right and

transverse colon, small bowel mesentry and duodenum were mobilized to the left to expose the retroperitoneal great vessels. The renal hilum was explored, and all suspicious nodes were biopsied. No nodal metastases were found on frozen section.

Dissection of the supraceliac bare area of the aorta

The liver was circumferentially mobilized to expose the retrohepatic vena cava by incising the triangular, falciform, and coronary ligaments. The diaphragm was split into the central tendon toward the inferior vena cava. Several short segmental veins between the dorsal surface of the liver and the vena cava were divided to expose the vena cava further. The hepatic artery and portal vein were exposed at the porta hepatis. The abdominal aorta was exposed at the supraceliac bare area by dividing the right crus of the diaphragm.

Mobilization of the right kidney, dissection and division of the renal artery

The kidney was mobilized partially posteriorly, and the renal artery was doubly ligated. This maneuver helps in minimizing significant shunting in many of the tumors. After division of the renal artery, dissection was carried superiorly to the right adrenal vein, which is located higher and posterior.

Right nephrectomy, cross-clamping of the inferior cavo-atrial junction, left renal vein, and intermittent cross-clamping of the supraceliac abdominal aorta

The abdominal aorta was cross-clamped at the supraceliac bare area. The clamp was intermittently applied approximately every 5 to 7 minutes to minimize ischemia of the hepatic and contralateral renal vascular bed and the lower torso. The distal inferior vena cava, the contralateral renal vein, and finally the intrathoracic vena cava were clamped, isolating the vena cava from all venous inflow except for pooled blood within the hepatic system. Subsequently, the vena cava was incised with an ellipse of cava around the renal vein ostium. The tumor thrombus was dissected using endarterectomy instruments and was extracted in continuity with the nephrectomy specimen. The individual hepatic veins and the IVC were completely cleared of thrombus. As soon as the tumor thrombus was removed en bloc, the aorta was released to restore circulation. A cardiotomy sucker was placed within the opened IVC, and the venous return was managed successfully. The IVC was flushed vigorously with cold saline.

In this patient, the tumor thrombus was occupying nearly half of the right atrial cavity. He required aortic cross-clamping, cardioplegic arrest, and clamping of the pulmonary artery to avoid tumor embolization. Tumor thrombectomy was performed through two separate incisions in the infrahepatic inferior vena cava and right atrium. After removing the tumor, the right heart chambers including the opened inferior vena cava were vigorously flushed with cold saline solution with the pulmonary arterial clamp in situ to wash away any residual tumor material.

Repair of the atriocaval junction and inferior vena cava

The cavotomy and the cavoatriotomy were repaired in two layers using 5-0 polypropylene (Johnson and Johnson Ltd., Ethicon, LLC, San Lorenzo, USA).

Weaning from cardiopulmonary bypass

During intermittent supraceliac clamping at 32°C, the systemic flow rates were maintained between 2.0 and 2.2 $L \cdot min^{-1} \cdot m^{-2}$ with a mean perfusion pressure between 60 and 80 mm Hg. Cardiopulmonary bypass was decreased and terminated after rewarming the patients, and heparin was reversed. We did not use an IVC clip or filter.

Short- and Long-term Results

Postoperative recovery was uneventful. The cumulative drainage was 350 ml in first 24-hours. There was no renal failure and no neurological deficit. Follow-up at 38^{th} month revealed the patient in New York Heart Association Functional Class-I with no evidence of any recurrence in any part of the body.

Conclusions

We conclude that mild hypothermic cardiopulmonary bypass, and intermittent occlusion of the supraceliac abdominal aorta is a reasonable approach for removal of renal cell carcinoma extending into suprahepatic level IV neoplastic extension. The advantages of this approach are avoidance of deep hypothermic circulatory arrest, reduced duration of cardiopulmonary bypass and therefore decreased perfusion related complications. The other highpoints are cardioplegic arrest, which allowed complete intra-atrial thrombectomy, clamping of the pulmonary artery to prevent tumor embolization into pulmonary arteries and combination of right atriotomy and infrahepatic vena cavotomy that allowed total removal of extensive intracardiac and vena caval tumor thrombi.

Declaration of Conflicting Interests

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