Original Article

A new classification of inferior vena cava thrombus in renal cell carcinoma could define the need for cardiopulmonary or venovenous bypass

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ABSTRACT

Introduction: Although the level of inferior vena cava (IVC) thrombus governs the type of surgical approach, there is no consistency in reporting the levels of IVC thrombus in the literature. This prospective study illustrates a simple three-level classification based on the need for clamping hepatoduodenal ligament and venovenous or cardiopulmonary bypass.

Materials and Methods: Between January 2010 and June 2014, 30 patients of renal mass with renal vein and/or IVC thrombus were treated after classifying the IVC thrombus into three levels on the basis of need for clamping the hepatoduodenal ligament. After excluding renal vein thrombi, level I was described as thrombus located caudal to the hepatic vein. Level II included all retrohepatic, suprahepatic infradiaphragmatic or supradiaphragmatic thrombi reaching till the right atrium. Atrial thrombi were categorized as level III. Level I and II thrombi were managed without venovenous or cardiopulmonary bypass. Level III thrombus required cardiopulmonary bypass.

Results: Of 26 patients with thrombus, 13 had level I thrombus. Of eight cases with level II thrombus, three were retrohepatic, three were suprahepatic infradiaphragmatic and two were supradiaphragmatic. All were removed successfully. Of five patients with level III thrombus, three were operated with cardiopulmonary bypass while the remaining two patients were too sick to be taken up for surgery. The median hepatoduodenal ligament clamp time was 10 min. One patient with level II thrombus had transient liver enzyme elevation.

Conclusion: Renal vein thrombus should not be categorized as level I thrombus. Level II thrombus, irrespective of its relation to the diaphragm, could be managed without venovenous or cardiopulmonary bypass.

Key words: Cardiopulmonary bypass, inferior vena cava thrombus, renal cell carcinoma, venovenous bypass

INTRODUCTION

Tumor thrombus in renal cell carcinoma (RCC) has a reported incidence of 4–10%, with a wide variation in description of level of thrombus, taking into account the diaphragm and the hepatic vein[1-5] [Table 1]. In a recently updated staging system by the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC), level of thrombus has been described as: T3a, renal vein involvement; T3b, inferior vena cava (IVC) thrombus extending below the diaphragm; and T3c, IVC thrombus extending above the diaphragm.[6] A contemporary review has shown the effect of levels on survival, but the level of this evidence is tenuous.[7] When adjusted for grade

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Table 1: Various classifications described for renal vein and IVC thrombus in renal cell carcinoma

	Renal vein	Infrahepatic		Above the liver edge but below the hepatic vein	Hepatic IVC	Suprahepatic infradiaphragmatic	Suprahepatic supradiaphragmatic	Atrium
		IVC <2 cm above the renal vein	IVC >2 cm above the renal vein					
Ciancio[9]	I	II		III a	III b	III c	III d	IV
Moinzadeh[2]		I					II	III
Neves[10]		I	II			III	IV	
Novick[11]	I	II					III	IV
Hinman[12]	I	II					III	
AJCC, UICC 2010[6]	T3a	T3b					T3c	
Present study		I			II			III

IVC=Inferior vena cava, AJCC=American Joint Committee on Cancer, UICC=Union Internationale Contre le Cancer

and stage of tumor, the level *per se* did not affect the survival.[8]

More than the survival, it is removal of the thrombus that demands surgical expertise. Technically, it is the hepatic vein that forms an important landmark for variation in the technical steps of thrombus extraction, as it involves the clamping of hepatoduodenal ligament when the thrombus reaches up to or above the level of hepatic vein insertion. Despite that, there is no uniformity in classifying IVC thrombus, which has been described in many ways taking the diaphragm and hepatic vein as landmarks [Table 1].[6,9-13]

Apart from the cephalad control of IVC, need for venovenous or cardiopulmonary bypass is not uniformly described. We prospectively evaluated the new classification of IVC thrombus to streamline the need for venovenous or cardiopulmonary bypass and liver mobilization.

MATERIALS AND METHODS

A total of 30 patients with renal mass and renal vein and/or IVC thrombus were prospectively studied from January 2010 to June 2014. Initial evaluation and staging of renal vein or IVC thrombus was performed on the basis of a contrast-enhanced computed tomography (CECT) scan and/or magnetic resonance imaging (MRI) of the abdomen and pelvis. Of 30 patients, 26 had IVC thrombus and four patients had renal vein thrombus only.

Classification based on hepatic vein as a landmark

MRI was carried out to determine the extent and nature of the thrombus and IVC wall involvement. We reclassify IVC thrombi into three levels depending on the need for clamping hepatoduodenal ligament. Renal vein thrombus was not included in level I thrombus.

Level I: Thrombus caudal to insertion of hepatic vein when IVC could easily be clamped cephalad to it [Figure 1].

Level II: All thrombi classified as retrohepatic, suprahepatic infradiaphragmatic or suprahepatic supradiaphragamatic IVC [Figure 2].

Level III: Thrombus extending into the right atrium [Figure 3].

Surgical technique

With modified Chevron incision, the tumor-bearing kidney was mobilized along with the renal vein containing thrombus. The caudate lobe of the liver was dissected by ligating short hepatic veins and the IVC at this level was mobilized circumferentially. Although this step is sufficient to deal with level I thrombus, it is a very crucial step for the higher levels of thrombi to reduce porta hepatis clamp time [Figure 4]. For extraction of level I thrombus, venous occlusion was obtained with the previously placed tourniquets over the cephalad IVC after clamping the IVC caudal to the renal vein and contralateral renal vein. Hepatoduodenal ligament clamping was not performed.

For level II thrombi, a cephalad clamp on IVC was placed by a direct subdiaphragmatic approach to IVC at the diaphragmatic hiatus for three cases of retrohepatic and three cases of suprahepatic and infradiaphragmatic thrombus under the guidance of transesophageal echocardiography (TOE) or surface ultrasonography. The median sternotomy and thoracotomy approach was adopted in two cases each for clamping the intrapericardial IVC. One of these two patients was operated in the cardiac theater, where the thrombus was reaching the atrium, and we could bring down the thrombus in the intrapericardial IVC by downward push to the liver for intrapericardial clamping of the IVC. All level II thrombi were managed without venovenous or cardiopulmonary bypass using TOE and surface Doppler probe except in one case, where neither of the facilities was functional during the surgery, which led to severance of the tip of the thrombus while applying the clamp, ultimately leading to thromboembolism and death of the patient. For thrombus extraction, sequence of clamping included caudal IVC first, then hepatoduodenal ligament and lastly contralateral renal vessels before finally putting a cephalad

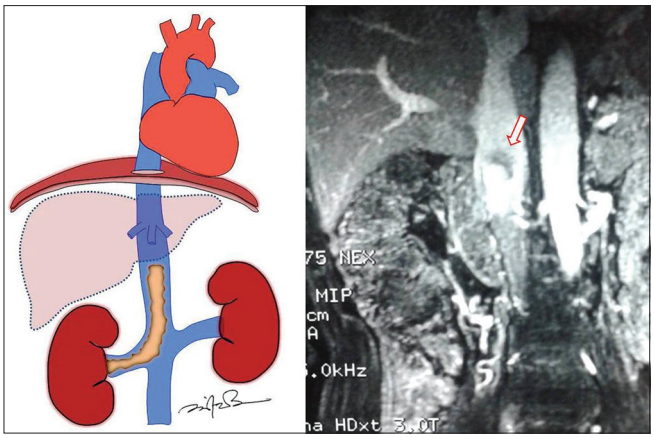

Figure 1: Level I thrombus (arrow indicating thrombus)

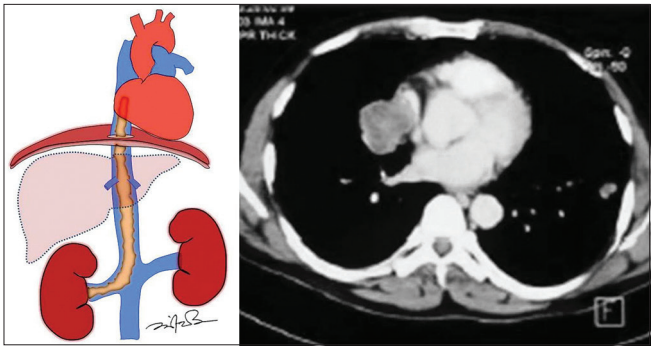

Figure 3: Level III thrombus with large thrombus in the atrium

clamp on the IVC. Level III thrombi were managed with cardiopulmonary bypass.

To save the porta hepatis clamp time, once the thrombus of level II and III were taken out, the IVC clamp that was cephalad to the hepatic vein was then repositioned proximal to the hepatic vein drainage at the level of the subhepatic IVC [Figure 4]. This helped in early release of the hepatoduodenal ligament. A drainage tube and chest tube were placed wherever needed.

No prior angioembolization was performed in any of our patients. Chevron incision gave a sufficient exposure even for large-sized tumors and a thoracoabdominal approach was avoided.

Need for liver mobilization

All level II and III thrombi were managed without mobilization of the liver, except one patient with level III thrombus, where the thrombus was attached to the IVC wall extending to hepatic vein insertion. MRI and intraoperative TOE were helpful in determining thrombus attachment to the IVC wall and its extent. As IVC wall involvement was found proximal to the hepatic vein insertion most of the time, liver mobilization was not required. Management strategy for the need of liver mobilization is given in Table 2.

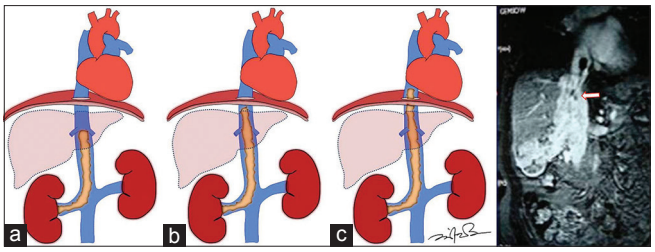

Figure 2: Level II thrombi. (a) Retrohepatic, (b) suprahepatic infradiaphragmatic and (c) suprahepatic and supradiaphragmatic thrombus (arrow indicating thrombus)

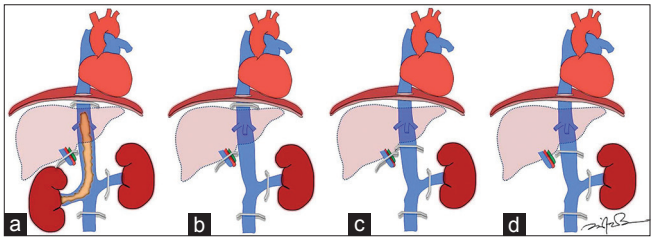

Figure 4: A cephalad clamp on the inferior vena cava (IVC) and clamp on the hepatoduodenal ligament (a).Once the thrombus is out, the cephalad clamp on the IVC is replaced to the subhepatic IVC (b and c) and then the hepatoduodenal ligament clamp is released (d)

TOE and surface ultrasonography

Simultaneous TOE and surface ultrasonography was performed to locate the tip of the thrombus, particularly at the time of applying a clamp. It also helped in detecting the blood flow around the thrombus. At times, when it was difficult to go caudal to the hepatic vein insertion, the surface Doppler probe was used to locate the distal end of the thrombus to avoid inadvertent clamping over the thrombus.

Total operative time, blood loss, hepatoduodenal ligament clamp time, intraoperative complications and post-operative renal and liver function tests were recorded.

RESULTS

Of 26 cases with IVC thrombus, 13 had level I thrombi. All these patients were managed successfully with mobilization of the infrahepatic IVC. Of eight cases of level II thrombi, three were retrohepatic, three were suprahepatic but infradiaphragmatic and two were supradiaphragmatic. All but one patient had successful removal of thrombus.

The median operative time and blood loss for level I and II thrombus was 200 min (160–240 min) and 230 min (220–280 min) and 800 mL (500–1200 mL) and 1100 mL (1000–1300 mL), respectively. The median hepatoduodenal ligament clamp time was 10 min (2–15 min). One patient had transient elevation of liver enzymes, which normalized within 1 week. In one patient with left renal tumor and level II thrombus, the right renal artery was clamped along with the renal vein. The warm ischemia time (WIT) in this patient was 10 min, with no rise of creatinine level post-operatively. Only one

Table 2: Management strategies for the three levels of IVC thrombus

Level of thrombus	Status on MRI	Cephalad IVC control	Venovenous or cardiopulmonary bypass
I	Subhepatic IVC thrombus	Caudate lobe mobilization	No
II	IVC wall is free	Subdiaphragmatic approach or thoracic approach (to clamp the intrapericardial IVC)	No
	IVC wall invasion is suspected extending up to the hepatic vein insertion	Liver mobilization technique	
III	Intra-atrial extension	Median sternotomy	Yes

IVC=Inferior vena cava, MRI=Magnetic resonance imaging

patient with level II thrombus had elevated creatinine level from 0.8 to 1.5 mg/dL [Table 3].

Of five patients with level III thrombus, only three patients were operated with cardiopulmonary bypass, while the remaining two patients were too sick to be taken up for surgery. Of the three operated patients, only two had successful outcome and one died of disseminated intravascular coagulation in the post-operative period. The median operative time and blood loss were 280 min (240–360 min) and 1400 mL (1200–2200 mL), respectively. The remainder of the complications is described in Table 3.

Table 3: Complication in patients with different levels of tumor thrombus

	Level I	Level II	Level III
Number	13	8	5
Acute renal failure requiring hemodialysis	0	0	0
Significant proteinuria requiring ACE inhibitors	1	1	0
Tumor embolism	0	1	0
Pneumonitis	1	0	0
Transient liver dysfunction	0	1	0
Chylous ascites	1	0	0
Perioperative death	0	1	1

ACE=Angiotensin converting enzyme

DISCUSSION

IVC thrombus possesses a unique challenge as it involves extensive dissection of the adjacent organs and transient control of circulation. The most important step in surgical management of thrombus is cephalad control of IVC. Although the level of extent of thrombus governs the type of approach, there is no consistency in reporting the levels of IVC thrombus in the literature.

Renal vein thrombus has been described as level I thrombus.[9,11,12] Similarly, a thrombus extending <2 cm within the IVC has also been described as level I thrombus, infrahepatic thrombus has been described as level II, infrahepatic IVC thrombus below the diaphragm has been described as level III and thrombus extending above the diaphragm has been described as level IV thrombus.[10,11] Another study has classified thrombus into three levels, which included infrahepatic thrombus as level I, thrombus above the hepatic veins but below the diaphragm as level II and thrombus at or above the level of the diaphragm as level III.[12]

There is not enough evidence to suggest that the level of IVC thrombus by itself affects survival in RCC. A recent study, based on retrospective analysis of patients from various centers, has shown that level II thrombus, i.e. thrombus below the diaphragm, and level III, i.e. thrombus above the diaphragm, has difference in survival after adjusting for lymph nodes and metastases. But, other important factors like cell type, perinephric fat invasion and performance status were not taken into account, despite the fact that the performance status is the single most predictive factor for survival in RCC. Similarly, perinephric fat involvement and cell type are two other important factors that affect cancer-specific survival and were not considered.

Without taking these confounding factors into account, assessment of impact of the different levels of thrombi on survival may not be appropriate. This would mean that in two different patients with similar confounding factors, level II thrombus that is suprahepatic but infradiaphragmatic portends worse survival once it grows further for 1 cm or so and crosses the diaphragm to become level III thrombus. At the same time, level I thrombus closer to the renal vein, when it grows for 4–6 cm in the IVC but remains below the hepatic vein, would not affect the survival as it is still classified as level I.

Therefore, until we prove that the level of thrombus itself affects the survival, classification should be based on surgical principles. Renal vein thrombus should not be classified as level I as it can be managed without cross-clamping the IVC. As any thrombus located at or above the hepatic vein insertion requires clamping of the hepatoduodenal ligament, the diaphragm should not be taken as a landmark to classify thrombus. Therefore, most of the thrombi in the IVC that are present below the insertion of hepatic vein should be classified as level I thrombi.

Thrombus at or above the insertion of hepatic vein, irrespective of whether it is above or below the diaphragm, till the entry into the atrium principally requires clamping of the hepatoduodenal ligament to prevent liver congestion. Such thrombi should be classified as 'level II' IVC thrombus. Conventionally, techniques described to treat thrombi above the hepatic vein and around the diaphragm involved complete liver mobilization and cardiopulmonary bypass with or without hypothermic circulatory arrest or venovenous bypass (VVB) by either open surgery or by the percutaneous method.[14-16] The problems with these two techniques are that cardiopulmonary bypass with hypothermia and use of heparin may result in platelet dysfunction and coagulopathy. This would increase the risk of bleeding, sepsis and multiorgan failure.[17-19] Cardiopulmonary bypass may also result in renal dysfunction in such patients who would be on one kidney, thereby increasing the chance for hemodialysis.[20,21] Complications like infection, vessel access injury and air embolism have also been reported with VVB.[15] Most of the thrombi, where cephalad clamp on the IVC could be applied, would not need any VVB or cardiopulmonary bypass. For level I thrombus, cardiothoracic back up is not required but for level II and III thrombus, it is always recommended to keep the back up support of a cardiothoracic surgeon.

The liver mobilization technique has been described by Ciancio *et al*. without the use of cardiopulmonary bypass or VVB.[22] In this technique, the liver was freed all around and left attached to the IVC with the hepatic vein; this technique was called the piggy back technique.[22] If the thrombus was above the diaphragm, then the piggy back technique was aided with an additional sternotomy or with a further modification described by the same authors for accessing intrapericardial IVC by the transdiaphragmatic approach.[9] In that approach, the IVC was mobilized at its hiatus in the diaphragm and the central tendon was incised to reach the right atrium.[9,22]

It may not always be necessary to mobilize the liver in such an extensive way. Caudate lobe mobilization is mandatory to put a sling at the subhepatic IVC for repositioning the suprahepatic clamp to the subhepatic level to reduce the hepatoduodenal ligament clamp time. Once it was ensured that the thrombus was not attached to the IVC wall by MRI, all the subtypes of level II thrombi could be managed without mobilization of the liver. But, in case of any suspicion of IVC wall attachment or if the patient has manifestations of the Budd Chiari syndrome, it would be better to mobilize the liver and expose the complete IVC.[9] In the present study, one patient with level III thrombus had thrombus attached to the IVC wall, extending to the hepatic vein for a distance of a few millimeters from the junction of the hepatic vein and IVC. The patient had his liver mobilized by the piggy back technique and was put on cardiopulmonary bypass.

MRI is the mainstay of imaging to determine the thrombus characteristics and its extent. IVC wall invasion could be diagnosed on MRI with 92% accuracy, and the most important indicator of diagnosing wall invasion is breach in laminar flow of blood due to extension of tumor into the wall.[23]

In one of our patients where the thrombus was just protruding into the atrium, a gentle caudal pull over the liver could bring the thrombus into the intrapericardial IVC and a clamp could be placed under the guidance of TOE, avoiding the need for VVB. This has also been described by other authors: To change the level by milking the thrombus down from the suprahepatic level to below the hepatic vein to reduce the hepatoduodenal ligament clamp time.[24]

Regarding hepatoduodenal ligament clamping, it has been shown in a randomized trial that the Pringle maneuver carried out for 20 min as normothermic clamping is not associated with any untoward hemodynamic changes or complications.[25,26] The median hepatoduodenal ligament clamp time in all our cases was 10 min, and only one patient had transient hepatic enzyme derangement who recovered spontaneously. None of our patients had any coagulation disorder. We do believe that repositioning the clamp to the subhepatic IVC to reduce hepatoduodenal ligament clamp time and applying the Satinsky clamp to reduce renal ischemia as described by Ciancio *et al*. would help in reducing post-operative complications.[22]

CONCLUSION

Evidence to prove that level of thrombus would affect survival is tenuous; therefore, it is the surgical principle of removing the thrombus that should form the basis of classification. Thrombus around the hepatic vein and diaphragm but not entering into the atrium should be classified in one group as they need clamping of the hepatoduodenal ligament and could be managed without venovenous or cardiopulmonary bypass. Thrombi that are not attached to the IVC wall and lying free in the IVC do not need liver mobilization either. The simple three-level classification described in this study will not only bring uniformity but also help in maintaining consistency in reporting surgical outcome and complications.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Hatcher PA, Anderson EE, Paulson DF, Carson CC, Robertson JE. Surgical management and prognosis of renal cell carcinoma invading the vena cava. J Urol 1991;145:20-4.

2. Moinzadeh 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.
3. Kim HL, Zisman A, Han KR, Figlin RA, Belldegrun AS. Prognostic significance of venous thrombus in renal cell carcinoma. Are renal vein and inferior vena cava involvement different? J Urol 2004;171:588-91.
4. Haferkamp A, Bastian PJ, Jakobi H, Pritsch M, Pfitzenmaier J, Albers P, *et al*. Renal cell carcinoma with tumor thrombus extension into the vena cava: Prospective long-term follow-up. J Urol 2007;177:1703-8.
5. Parekh DJ, Cookson MS, Chapman W, Harrell F Jr, Wells N, Chang SS, *et al*. Renal cell carcinoma with renal vein and inferior vena caval involvement: Clinicopathological features, surgical techniques and outcomes. J Urol 2005;173:1897-902.
6. Edge SB, Compton CC. The American Joint Committee on Cancer: The 7th edition of the AJCC Cancer Staging Manual and the Future of TNM. Ann Surg Oncol 2010;17:1471-4.
7. Martinez-Salamanca JI, Huang WC, Millan I, Bertini R, Bianco FJ, Carballido JA, *et al*. Prognostic Impact of the 2009 UICC/AJCC TNM Staging System for Renal Cell Carcinoma with Venous Extension. Eur Urol 2011;59:120-7.
8. Mejean A, Oudard S, Thiounn N. Prognostic factors of renal cell carcinoma. J Urol 2003;169:821-7.
9. Ciancio G, Shirodkar SP, Soloway MS, Livingstone AS, Barron M, Salerno TA. Renal carcinoma with supradiaphragmatic tumor thrombus: Avoiding sternotomy and cardiopulmonary bypass. Ann Thorac Surg 2010;89:505-10.
10. Neves RJ, Zincke H. Surgical treatment of renal cancer with vena cava extension. Br J Urol 1987;59:390-5.
11. Novick AC, Streem SB, Pontes E. Stewart's Operative Urology. 2nd ed. Philadelphia: Williams and Wilkins; 1989.
12. Hinman F. Atlas of Urologic Surgery. 2nd ed. Philadelphia: WB Saunders Co; 1998. p. 1172.
13. Blute ML, Leibovich BC, Lohse CM, Cheville JC, Zincke H. The Mayo clinic experience with surgical management, complication and outcome for patients with renal cell carcinoma and venous tumor thrombus. BJU Int 2004:94;33-41.
14. 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.
15. Obadia JF, Clavel JP, Bonnefoy E, Durand-Dubief A, Chassignolle JF. Surgery for caval atrial extension of renal malignant tumors using a venovenous shunt. Br J Urol 1997;80:812-4.
16. Browning AJ, Eardley I, Joyce AD, Minhas S, Bellamy MC. Percutaneous venovenous bypass in surgery for renal cell carcinoma with associated vena caval tumor thrombus. BJU Int 1999;83:850-2.
17. Stewart JR, Carey JA, McDougal S, Merrill WH, Koch MO, Bender HW Jr. Cavoatrial tumor thrombectomy using cardiopulmonary bypass without circulatory arrest. Ann Thorac Surg 1991;151:717-22.
18. Langenburg SE, Blackbourne LH, Sperling JW, Buchanan SA, Mauney MC, Kron IL. Management of renal tumors involving the inferior vena cava. J Vasc Surg 1994;20:385- 8.
19. Novick AC, Kaye MC, Cosgrove DM, Angermeier K, Pontes JE, Streem SB. Experience with cardiopulmonary bypass and deep hypothermic circulatory arrest in the management of retroperitoneal tumors with large vena cava thrombi. Ann Surg 1990;212:472- 6.
20. Di Mauro M, Gagliardi M, Iacò AL, Contini M, Bivona A, Bosco P, *et al*. Does off-pump coronary surgery reduce postoperative acute renal failure? The importance of preoperative renal function. Ann Thorac Surg 2007;84:1496-502.
21. Abu-Omar Y, Ratnatunga C. Cardiopulmonary bypass and renal injury. Perfusion 2006;21:209-13.
22. Ciancio G, Hawke C, Soloway M. The use of liver transplant technique to aid in the surgical management of urological tumors. J Urol 2000;164:665-72.
23. Aslam Sohaib SA, Teh J, Nargund VH, Lumley JS, Hendry WF, Reznek RH. Assessment of tumor invasion of the vena cava wall in renal cell carcinoma cases by magnetic resonance imaging. J Urol 2002;167:1271-5.
24. Ciancio G, Vaidya A, Savoie M, Soloway M. Management of renal cell carcinoma with level III thrombus in the inferior vena cava. J Urol 2002;168:1374-7.
25. Man K, Fan ST, Ng IO, Lo CM, Liu CL, Wong J. Prospective evaluation of the Pringle maneuver in hepatectomy for liver tumors by a randomized study. Ann Surg 1997;226:704-13.
26. Belghiti J, Noun R, Zante E, Ballet T, Sauvanet A. Portal triad clamping or hepatic vascular exclusion for major liver resection. A controlled study. Ann Surg 1996; 224:155-61.