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Kidney Cancer

Nephron-Sparing Surgery for Renal Cell Carcinoma: Detailed Analysis of Complications Over a 15-Year Period

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Abstract

Purpose: To assess the incidence of complications of conservative renal surgery for renal cell carcinoma in both elective and imperative indications, and its evolution over a 15 year period.
Patients and methods: From 1988 to 2003, 127 patients underwent partial nephrectomy or tumorectomy for renal cell carcinoma in our department. Indications were imperative in 42% ($n = 53$) and elective in 58% ($n = 74$) of cases. Morbidity was retrospectively assessed according to four parameters: 1- Period of surgery: A, from 1988 to 1999 and B, from 2000 to 2003. 2- Indication: elective vs. imperative. 3- experience of surgeon: senior vs. junior. 4- Nature of complications: minor or major. Comparative analysis was conducted using Chi-square and Fischer exact tests.
Results: Global incidence of complications was 30.7% ($n = 39$) corresponding to 18.1% minor ($n = 23$) and 12.6% ($n = 16$) major complications. Results show a moderate decrease of complication rate during Period B: 28.1% versus 32.9% during period A ($p = 0.69$). Complications occurred more frequently in imperative indications (49.1%) than in elective indications (17.6%) ($p = 0.002$), mostly regarding major complications (respectively 28.3% and 1.4%. ($p < 0.001$)). Overall re-intervention rate was 15.7%: 22.6% in imperative and 10.8% in elective indications ($p = 0.008$). Mean length of hospital stay was 14.1 days and significantly longer during period A ($p = 0.003$) and in imperative indications ($p = 0.009$).
Conclusion: In our study, conservative renal surgery has a significant rate of complications which is extremely variable regarding to different parameters. Most discriminating factor was indication: in imperative indications, we observed a high rate of major complications (28.3%) that we consider acceptable to prevent anephria in clearly informed patients.

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Major complications are exceptional in elective indications. Decreased incidence of complications during the later period (B) is modest, and the role played by systematic pedicular clampage is discussed. As results published in medical literature are difficult to compare, we agree with authors who recently proposed to standardize complications data analysis, using a gravity scale, in order to provide relevant information to patients about statistical risks before surgery.

1. Introduction

Conservative surgery for renal cell carcinoma, since its first description [1], has been widely diffused and performed in the last 15 years, and showed excellent oncological results in imperative and then elective indications [2–8]. It is also established that NSS lowers the risk of evolution towards chronic renal insufficiency compared to radical nephrectomy [9]. However, a recent study underlined that results published in medical literature regarding morbidity of conservative surgery are extremely variable, due to the lack of standardization [10]. As patients have to be clearly informed on surgical risks, especially in elective indications, it seems primordial to know precisely the morbidity of conservative surgery. To assess the benefit brought to patients through this procedure, we report morbidity observed in our institution over a 15 year period of conservative surgery.

2. Patients and methods

From 1988 to 2003, 127 patients underwent conservative surgery for renal cell carcinoma in our institution. Indications were imperative in 42% ($n = 53$) as tumors were bilateral ($n = 33$) or in solitary kidney ($n = 20$) and elective in 58% ($n = 74$) of cases (healthy contralateral kidney). We retrospectively recorded complications that occurred after surgery, using the following classification based on gravity and frequency of events:

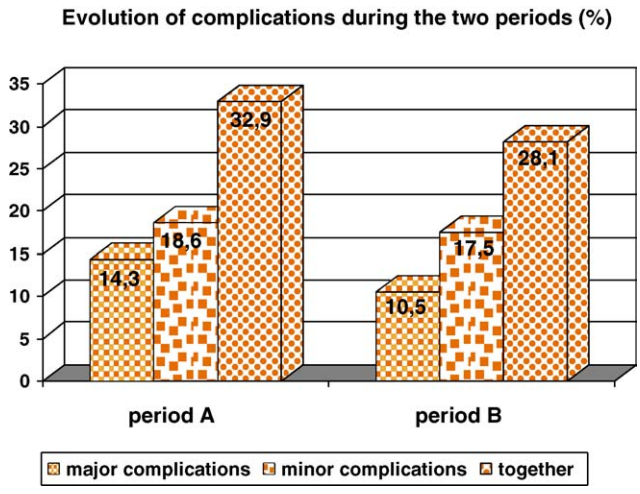
- *Minor complications*: urinary fistula, small (<4 cm) perinephric haematoma (not requiring reintervention), medical minor events as bacteriuria, lower limb deep venous thrombosis, respiratory infection.
- *Major complications*: death, acute renal failure, hemorrhage, deep abscess, bowel wound and all events leading to Intensive Care Unit or re-intervention.

All patients underwent ultrasonographic examination 7 days after surgery: if imaging revealed peri-renal urine effusion, patients underwent retrograde uretero-pyelography examination to confirm urine extravasation and subsequently insert ureteral stent if necessary.

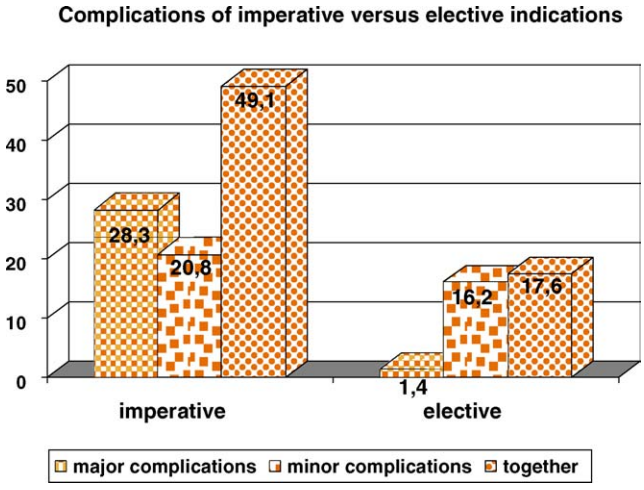
To assess morbidity time-related evolution, we divided our experience into 2 periods: period A from January 1988 to December 1999 ($n = 70$) and period B from January 2000 to December 2003 ($n = 57$). We adopted at our institution since year 2000 (period B) the protocol described at Cleveland Clinic including Mannitol perfusion of the isolated kidney before arterial occlusion, removal of the tumor during cold ischemia and if necessary Methylen color test to improve closure of the collecting system [4]. This operative procedure was followed each time reconstruction of the collecting system was expected. During period A, the operative technique was not standardized and only depended on the habits of the surgeon, so that it could include parenchymal or pedicle clamping or not, and ureteral stent placement or not. The only common point of all interventions of period A is that there was no use of cold ischemia nor methylen blue test. In this series all interventions were performed by open surgery. Thirteen different surgeons performed the 127 procedures and were divided into 2 groups: 5 of them performed 112 procedures (88.1%) and were designed as senior surgeons. The 8 other surgeons preformed 15 procedures (11.9%) and were designed as junior surgeons. Thus, morbidity of conservative surgery were compared regarding to 4 parameters: period A or B, indication (imperative vs. elective), experience of surgeon (senior vs. junior) and nature of complications (minor vs. major). The incidences of urinary fistula and acute renal failure, as these are specific complications of conservative surgery, were also reported. Comparative analysis was conducted according to Chi-square and Fischer exact tests, and validated by our department of biostatistics.

3. Results

Overall rate of complications was 30.7% ($n = 39$). Rate of complications was respectively 32.9% and 28.1% during period A and B ($p = 0.69$), 49.1% and 17.6% in imperative and elective indications ($p = 0.002$), 31.2% and 26.7% for senior and junior surgeons respectively ($p > 0.9$) (Histograms 1–3). Regarding their nature, we report 12.6% of major and 18.1% of minor complications detailed in Table 1. Most frequent major event was acute renal failure (5.4%, $n = 7$) whereas urinary fistula (10.1%, $n = 13$) was the most frequent minor complication. Urinary fistula occurred independently from period (11.4% in period A and 8.7% in period B), indication (11.3% versus 9.4% for elective), or experience of the surgeon (10.7% for senior versus 6.7% for junior). One patient died 2 months after surgery from acute

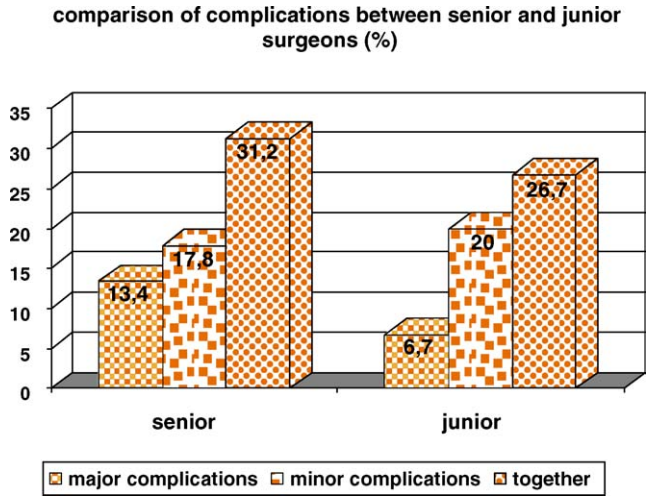


Histogram 1 – Evolution of complications during the two periods.



Histogram 2 – Complications for imperative versus elective indications.

hemorrhage on the remaining half kidney; as he had recent history of heart transplant, this patient was under heavy immunosuppressive and anticoagulation treatment. The decrease of overall complications from period A to period B (32.9% to 28.1%) is mainly due to decrease of major complications



Histogram 3 – Complications for senior versus junior surgeons.

(14.3% to 10.5%. $p = 0.59$). Morbidity occurring in imperative indications was significantly higher than in electives (49.1% vs. 17.6%, $p = 0.002$). Only one patient (1.4%) had major complications in elective indication (acute hemorrhage treated by embolization) whereas major events occurred in nearly one third of patients in imperative indications (28.3%, $p < 0.001$).

20 patients (15.7%) experienced re-intervention: 12 ureteral stents were endoscopically inserted,1 embolization for hemorrhage was necessary, and 7 open surgery were performed because of acute hemorrhage ($n = 1$), necrosis of remaining ipsilateral kidney ($n = 1$), major urinary collection in retroperitoneum ($n = 1$), wall infection ($n = 1$), acute necrotizing pancreatitis ($n = 2$) and bowel perforation ($n = 1$). Re-intervention rate was two times higher in imperative than in elective indications (22.6% vs. 10.8%. $p = 0.08$), but no significant difference was observed between period A and B (17.1% and 14%).

Mean length of hospital stay (LHS) was 14.1 days (6 to 90). It was longer in Period A (15.8 days) than in period B (12.2 days) ($p = 0.003$), and longer in imperative (17.6 days) than elective (11.6 days)

Table 1 – Details of complications

Major complications - *n* (%)		Minor complications - *n* (%)	
Acute renal failure	7 (5.4)	Urinary fistula	13 (10.1)
Intra-abdominal lesion requiring re-intervention	4 (3.2)	Retroperitoneal collection	5 (4)
Hemorrhage	3 (2.4)	Minor medical complication	5 (4)
Remnant necrosis	1 (0.8)		
Death	1 (0.8)		
Total	16 (12.6)		23 (18.1)

Table 2 – Main characteristics of tumors of elective versus imperative group

	Elective indications	Imperative indications	*p*
Mean tumor size (cm) (min-max)	2.8 (1–12)	4.1 (1.1–9.5)	<0.0001
Tumor location (*n* - %)			
Superior pole	22 (29.7)	13 (26.5)	0.1
Mediorenal	18 (24.3)	10 (20.4)	
Inferior pole	26 (35.1)	12 (24.5)	
Hilar	5 (6.7)	5 (10.2)	
Multifocal	3 (4)	9 (18.3)	
Total	53	74	
Mean operative time (min)	129	177	0.0002

indications ($p = 0.009$). When major complication occured, LHS was 26.7 days whereas LHS was 17.7 days when only minor complications occured. Among the 13 patients with urinary fistula and the 7 patients with acute renal failure, mean LHS was respectively 20.7 and 19.8 days.

The main characteristics of tumors of elective versus imperative group are exposed in Table 2.

4. Discussion

As almost one third of patients presented with complications, our study underlines that morbidity after conservative surgery for renal cell carcinoma is a significant issue and has to be clearly notified to patients prior to surgery. However, our results show that the expected rate of complications is variable regarding different parameters. Most discriminating and significant factor is indication. Not only imperative indications are associated with higher rate of complications (49.1% vs. 17.6% in elective indications), but complications that occurred in imperative indications are mainly major events. On the opposite, 92% of complications in elective indications are minor events and no patient had to undergo re-intervention nor intensive care. In our study, only one major complication was observed in elective indication, and was treated by embolization. Thus, it seems reasonable to assess that major complications are exceptional in elective indications [11].

Did outcome improve from 1988 to 2003 in our experience? As morbidity rate was 32.9% prior to 2000 (period A) and 28.1% after 2000 (period B), we report a moderate non significant decrease of overall complications ($p = 0.69$). Rate of major complications decreased from 14.3% to 10.5% ($p = 0.59$), whereas rate of minor complications is comparable in both period A and B. Main technical evolution in period B was the use of the protocol described at Cleveland Clinic when reconstruction of urinary tract was expected [4]. According to the authors, this technique allows better assessment of surgical margins, control of hemostasis, urinary tract suture and prevent from post operative acute renal failure and ischemia-reperfusion injury. We actually followed this protocole for 26% of procedures in period B and thus, we still consider that our follow up and number of procedures are for instance to limited to conclude about its efficacy. The decrease of major complication rate is then probably due rather to a global learning curve effect but considering Histogram 3, we notice that experience of surgeon had no influence on complications. The mentioned ''senior surgeons'' had each performed around 30 procedures at the end of the studied periods and we can imagine that the benefit of experience appears after more procedures than that. As the type of indication appeared to be the most significant factor of complication, we analyzed the different features of these two groups (Table 2): mean tumor size and mean time of intervention were statistically different between the two groups but only the size of tumors appeared to be involved when considering the probability of complication ($p < 0.0001$). The locations of tumors were comparable between the two groups ($p = 0.1$) and did not influence the rate of complications ($p = 0.9$). Urinary fistula and acute renal failure are known to be the most frequent complications in conservative renal surgery [4,12–16]. Our results are conform to this statement. Though a moderate decrease of the incidence of urinary fistula from period A to B, 11.4% versus 8.7% ($p = 0.8$), the 10.1% rate of urinary fistula of the whole series is quite high, regards to other recents series [10,17–19]. The systematic ultrasonographic examination 7 days after surgery probably contributed to surestimate this complication leading to 12 of the 20 reinterventions mentionned, even in non symptomatic cases. A less agressive attitude with no systematic ultrasonography and no systematic ureteral stenting in case of urinoma could be advocated, resulting in a lower rate of urinary fistula and reintervention rate.

In our study, risk of post-operative acute renal failure is 13.2% in imperative indications. In one case, acute renal failure led to terminal renal insufficiency. Renal failure is responsible for a slight non-significant increase of the mean length of hospital stay (19.8 days); indeed, most of acute renal failure we observed were due to acute tubular necrosis and were rapidly regressive with a treatment by consequent hydration and nephrotoxicity prevention. We emphasize that, in elective indications, no renal failure was observed and mean length of hospital stay was significantly shorter than in imperative indications.

Rate of morbidity reported in literature is variable, ranging from 4 to 37% [3,10,12,13,15,17,20]. This disparity is partially explained by the different proportion of elective indications as studies with majority of imperative indications report more than 20% of complications [13,15,19,21,22] whereas morbidity reported in studies with majority of elective indications range from 0 to 12% [14,17,23–26]. Moreover, rate disparity is clearly due to the absence of data analysis standardization: authors do not include the same event as complications and non exhaustiveness of event report is a known bias of retrospective studies. Thus, a recent prospective (but not randomized) study on a large cohort with more than 80% of elective indications report 19% of complications after conservative surgery including 9% of procedure related complications. Authors underline that, though there is no difference in overall morbidity rate after radical and conservative surgery, a significant difference exists if they analyze only specific procedure related complications. They also propose a seducing standardized complication grading scale which allows to define precisely major and minor events, and specific complications related to conservative surgery [10]. It is suitable to us that other authors report their results after conservative surgery using the same scale.

5. Conclusion

The contribution of conservative surgery in the management of renal cell carcinoma is well known in both elective and imperative indications. This conservative approach corresponds to a satisfying attitude also developped in others specialities like breast or limbs surgery [27–30]. Partial nephrectomy and tumorectomy allows an effective cancer control with the advantage of sparing nephrons [31–33]. Conservative surgery is particularly indicated as well for the treatment of incidentally little tumors, so far as up to 20% of them are benign tumors [34,35]. Moreover, in the same idea of minimal invasion and kidney preservation, laparoscopic approach is being developed [24]. Our results, as well as those reported in literature, show that morbidity of conservative surgery is not negligible and certainly disparate regarding different parameters. In our experience, most discriminating factor of variation is indication: in imperative indication, we observed a high rate of major complications (28.3%) that we consider acceptable to prevent anephria in clearly informed patients whereas one patient only in elective indication (1.4%) presented with major complications.

Information given to patients is primordial as major complications are hardly acceptable in elective indications; it implies to provide practitioner with reliable information based on prospective studies with a standardized complication grading scale that allows an objective statement of morbidity of conservative surgery. Knowledge of detailed morbidity also permits patients selection and puts into balance, case by case, the advantages of nephron sparing surgery with the risk of procedure related complications.

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