



Persistent orchialgia after laparoscopic living-donor nephrectomy: an underestimated complication requiring information adjustment

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Abstract

Purpose Laparoscopic living-donor nephrectomy (LLDN) is the gold-standard procedure for kidney procurement. Ipsilateral orchialgia has barely been described. Some authors reported that ligation of gonadal vein (GV) above iliac vessel bifurcation could prevent orchialgia. We aimed to assess incidence and duration of orchialgia after LLDN in male donors despite distal ligation of GV.

Methods Patients who underwent LLDN from 2014 to 2017 were included. Standard procedure consisted in distal ligation of GV, close to the renal vein confluence and proximal ureteral ligation. Patients' demographics, per-operative data, and post-operative consultation reports were retrospectively reviewed. Orchialgia and scrotal symptoms were assessed through a non-validated questionnaire by phone interview.

Results Sixty-nine donors were included. Orchialgia incidence and testicular swelling were 31.9% ($n = 22$) and 15.9% ($n = 11$), respectively. Median symptom duration was 15.5 months. Orchialgia led to medical consultation in 41.7% ($n = 10$) of cases. All patients declared having been informed, prior to donation, about possible residual pain but not specifically orchialgia.

Conclusion Orchialgia after LLDN affects more than 30% of donors, despite distal ligation of GV and led less than 50% of them to medical consultation, suggesting a large underestimation in clinical practice. Emphasis should be put on this complication during pre-donation information.

Keywords Living donor · Laparoscopic donor nephrectomy · Renal transplantation · Testicular swelling · Orchialgia · Post-operative outcome

Abbreviations

GV Gonadal vein
LLDN Laparoscopic living-donor nephrectomy

Introduction

Since its first description 20 years ago by Ratner et al. laparoscopic procedure has become the gold standard for living-donor nephrectomy [1–3]. Despite its low morbidity rate, complications were reported [4–6]. Post-operatives main complications are wound complications, chest infections, and less frequently evolution to chronic kidney failure [7, 8]. Laparoscopic living-donor nephrectomy (LLDN) has a major complication rate of 1–6% and a minor complication rate of 10–30% [4, 8–10]. Following laparoscopic nephrectomy, ipsilateral orchialgia have also been reported [11, 12]. Accordingly, it was also described for LLDN with incidence varying from 8 to 44% of the cases [13, 14]. The aetiopathogenesis of orchialgia in these cases is not clear with three main suspected aetiologies: vascular congestion due to ligation of the gonadal vein (GV), testicular ischaemia caused by testicular artery disruption, and neural injury to

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the spermatic plexus. It has been suggested that ligation of the GV above the iliac vessels bifurcation could prevent this complication [13, 15]. In a controlled study by Sureka et al. living donors were randomized in two groups: ligation of the GV above or below iliac vessels bifurcation, respectively [15]. No patient from the first group had orchialgia, whereas 9 patients developed ipsilateral orchialgia in the group where GV ligation was below iliac vessels bifurcation.

The aim of our study was to assess the incidence and duration of orchialgia after LLDN in male donors despite distal ligation of GV, close to the renal vein confluence, and proximal ureteral ligation.

Materials and methods

Patients

We conducted a single-center retrospective study by reviewing files and computer database to include male patients who underwent LLDN between January 2014 and July 2017. All patients gave their consent for research and use of their medical data. Patient's demographics and per-operative data were collected. We reviewed testicular antecedents including epididymitis, inguinal hernia, testicular ectopia, and any inguino-scrotal surgery. The local ethics committee approved the study and all patients gave their informed consent for the use of their clinical data.

Patient information delivery

Before surgery, the surgeon gave all information to the patient about the procedure during a dedicated consultation including the surgical technique, length of stay at the hospital, adverse events, complications, and regular follow-up. During this consultation, no oral information was given to the patients about post-operative testicular pain as, before this study, we were not aware of its potential high rate. Main information was listed in a specific form developed for LLDN and written by the French Association of Urology (AFU) which was always given to patient. In that form, post-operative testicular pain was not mentioned.

Surgical procedure

Living-donor nephrectomy was performed following the same standardized transperitoneal laparoscopic procedure by two surgeons with more than 7 years of expertise. The left kidney was preferentially removed whenever anatomic and functional features were favorable (vessels number and length, kidney size and trophicity, and renal function according to scintigraphy). Patients were positioned on lateral decubitus with strict checking of all support points,

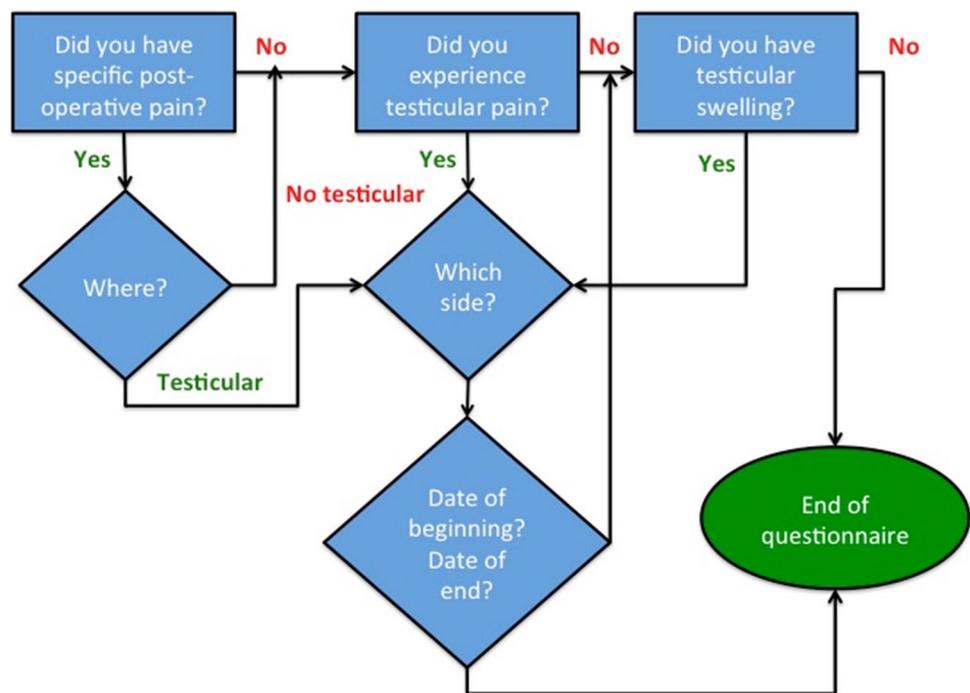
including scrotal release from both thighs. We used a four-port technique with hand-assisted device (GelPort laparoscopic system®), which allowed preparing the ipsilateral iliac incision to minimize kidney procurement and warm ischemia times. Renal artery was dissected close to the aorta to optimize vessel length. Renal vein was dissected; gonadal vein and adrenal vein were ligated before their confluence with the left renal vein. Ligation of GV was systematically above iliac vessel bifurcation, at the kidney lower pole, close to the renal vein confluence (less than 1 cm). Gonadal artery was not dissected and was never seemed to be sectioned. The kidney was then released with a simple nephrectomy dissection plane. At our center, we systematically performed (except in the case of vesicoureteral reflux nephropathy in the recipient) pyelo-ureteral anastomosis. Thus, a short ureteral segment is sufficient, which is why the section of the ureter was always above its crossing with the iliac vessels. Renal artery was sectioned after a single ligature proximal to the aorta, following by renal vein section according to the same technique in front of the aorta. The kidney was hand-removed through the iliac incision and prepared on a back table by another team. In our routine procedure, a Blake drain was positioned at the end of the procedure in the nephrectomy bed, through the 5 mm aid trocar hole. The drainage was removed at day 1 or 2, and the bladder catheter was removed at day 1 for all patients. Patients were discharged between day 3 and day 5 with the same non-opioid analgesic treatment (paracetamol and phloroglucinol) during 7 days and received a certificate of absence from work for a month to recover.

Symptoms' evaluation

We developed a non-validated phone questionnaire (Fig. 1), which assessed post-operative orchialgia, testicular swelling, pain duration, and interval time between surgery and orchialgia occurrence. The same investigator called all the donors and conducted the same structured interview, following a pre-defined order, as shown in Fig. 1. Testicular symptoms were assessed by a standardized phone interview once on July 2018. Patient was asked if he had experienced any specific post-operative pain. In a second step, patient was asked if any scrotal pain had occurred, how long it lasted, and whether he needed medical consultation or analgesic treatment. Moreover, patient was asked if the pain delayed return to work. In addition to the questionnaire, post-operative consultation reports were reviewed to collect orchialgia or testicular swelling events. Likewise, we reported scrotal Doppler ultrasound, when performed to investigate testicular events.

The primary endpoint of our study was post-operative orchialgia occurrence. Secondary endpoints were testicular

Fig. 1 Telephone questionnaire. We developed a non-validated questionnaire which assessed post-operative orchialgia, testicular swelling, pain duration, and interval time between surgery and orchialgia occurrence. Each male donor was called by the same investigator. Specific questions were asked following a pre-defined order as shown in the figure



swelling, duration of orchialgia, and medical consultation for testicular issues.

Statistical analysis

Categorical variables were expressed in numbers (with percentage). Continuous variables were expressed in mean (\pm standard deviation, SD) or median (with minimum and maximum data) and analyzed using unpaired Student's *t* test. Qualitative variables were analyzed using Fisher's exact test two-tailed. Statistical significance was defined as $p < 0.05$. The statistical analysis was performed using Prism software ©.

Results

From January 2014 to July 2017, 79 males underwent LLDN. We could contact 69 patients who all accepted to answer the questionnaire. Left and right LLDN were performed for 65 (94.2%) and 4 (5.8%) patients, respectively. Patients' demographics and per-operative data are reported in Table 1.

Among the 69 patients, 22 (31.9%) had post-operative orchialgia. Eighteen patients (26.1%) reported ipsilateral pain corresponding to the large majority of all reported orchialgia (81.8%) (Table 2). Median delay between surgery and orchialgia occurrence was 1 month [0.25–6]. Median orchialgia duration was 15.5 months [1–36]. Testicular swelling was also reported by 11 patients (15.9%) (Table 2).

Table 1 Patient demographics and per-operative data

	Patients (n = 69)
BMI [(kg/m ²), mean (\pm SD)]	26.2 (\pm 2.1)
Age [(years), mean (\pm SD)]	52.3 (\pm 12.9)
Testicular antecedent [n (%)]	7 (10.1%)
LLDN side [n (%)]	
Left	65 (94.2%)
Right	4 (5.8%)
Operating time [(min), mean (\pm SD)]	115.9 (\pm 26.8)
Blood loss [(ml), mean (\pm SD)]	10.1 (\pm 36.9)
Serum creatinine value [(μ mol/l), mean (\pm SD)]	
Pre-operative	97.5 (\pm 13.4)
Post-operative ^a	122.9 (\pm 16.9)

^aPost-operative serum creatinine value was defined at 1 month following nephrectomy

No symptoms were concomitant neither with fever nor with functional urinary signs, excluding any cause of epididymis.

Among 24 patients reporting post-operative scrotal symptoms (pain or swelling), 10 (41.7%) asked for medical consultation at our transplantation center. For two patients, clinical exam revealed left hydrocele; there were no other abnormalities. Scrotal Doppler ultrasound was performed for 8 patients based on pain intensity, pain duration or clinical abnormalities: 2 for hydrocele at physical examination, 3 for testicular swelling, 1 for chronic testicular pain, and 2 for acute or growing scrotal pain. Adequate testicular blood supply was confirmed on each ultrasound and there was no

Table 2 Post-laparoscopic living donor nephrectomy testicular events

	Patients (<i>n</i> = 69)
Testicular events	24 (34.8%)
Orchialgia [<i>n</i> (%)]	22 (31.9%)
Ipsilateral	18 (81.8%)
Contralateral	2 (9.1%)
Bilateral	2 (9.1%)
Testicular swelling [<i>n</i> (%)]	11 (15.9%)
Ipsilateral	10 (90.9%)
Contralateral	1 (9.1%)
Bilateral	0 (0%)
Medical consultation for testicular symptoms [<i>n</i> (%)]	10 (41.7%)

varicocele. For two patients, left hydrocele was found on ultrasound.

Among 22 patients with post-operative scrotal pain: 8 (36.4%) did not receive specific treatment, 8 (36.4%) used non-opioid analgesic (paracetamol, phloroglucinol), 3 (13.6%) received nonsteroidal inflammatory drugs (NSAIDs), 1 (4.5%) patient receives neuropathic treatment (amitriptyline), and 2 patients (9.1%) were not able to answer this question.

Considering patient characteristics and per-operative data, there was no significant difference between the patients reporting post-operative scrotal symptoms and the patients without any post-operative scrotal symptom (Table 3).

We asked every patient about pre-operative information: all mentioned having been correctly informed during the pre-LLDN consultation about the main risks and residual abdominal pain. However, all reported not having been informed on possible post-operative orchialgia.

Finally, among 24 patients reporting post-operative scrotal symptoms, 3 (12.5%) had to delay their return to work because of testicular pain.

Discussion

In our study, ipsilateral orchialgia following LLDN occurred for more than 25% of our patients (26.1%). Considering any testicular event (testicular swelling or orchialgia), almost 35% of donors were concerned (34.8%). Our high rates contrast with the literature: according to Kim et al., Srivastava et al., and Shirodkar et al. male donors were affected in 9.6%, 8.5%, and 6.2% of the cases, respectively [11, 13, 16]. In their systematic review, Kortram et al. reported 0.6% of testicular swelling, pain or epididymitis [17]. Despite a higher number of patients in these studies, the reports were also retrospective, and our study is the first to investigate scrotal events using a specific questionnaire and individual patient phone call. Generally, post-operative pain are often underestimated; more specifically in living donors [18]. We believe that the increase rate of scrotal pain in our study is explained both by our comprehensive investigation of post-operative pain in that population and both by our long patients' follow-up.

Our results also suggest an underestimation of orchialgia following LLDN as less than half of patients (41.7%) suffering from testicular symptoms asked for medical consultation.

Post-nephrectomy orchialgia mechanism is poorly understood. It has been suggested that per-operative GV ligation led to testicular vascular congestion and pain [12]. In the same study, Gjertson et al. suggested that interruption of the lymphatic drainage contributed to orchialgia. This is consistent with testicular pain due to varicocele and low blood flow. However, low residual pain following varicocele treatment may suggest that other factors are involved [19, 20].

Two patients had hydrocele associated with orchialgia in our study for whom no specific etiology was evidenced such as infection or traumatism. One could compare hydrocele occurrence following LLDN where GV is ligated with hydrocele following varicocele management by embolization. In a recent meta-analysis, Silay et al. evaluated 16 130

Table 3 Comparison between patients with or without post-LLDN scrotal symptoms

	Scrotal symptom	No scrotal symptom	<i>p</i> value
Patients (<i>n</i>)	24	45	
Body mass index [(kg/m ²), mean (±SD)]	25.4 (±2.9)	25.4 (±3.7)	0.97
Age (years) [mean (±SD)]	49.7 (±10.4)	53.7 (±14)	0.23
Testicular antecedent (<i>n</i>)	1 (4.1%)	6 (13.3%)	0.41
Epididymitis	1	0	–
Bilateral hernia cure	0	2	–
Right hernia cure	0	2	–
Left hernia cure	0	0	–
Non-treated bilateral ectopia	0	1	–
Treated bilateral ectopia	0	1	–
Operating time [(min), mean (±SD)]	110.5 (±22.1)	118.5 (±28.8)	0.27
Blood loss [(ml), mean (±SD)]	10 (±30.8)	3 (±16.4)	0.25

patients who underwent varicocele treatment [21]. Hydrocele ranged from 0 to 12% and lymphatic sparing management significantly decreased hydrocele rates ($p=0.02$) with an OR 0.08 (95% CI [0.01, 0.67]). Consequently, we could assume and conclude that GV ligation with increased venous pressure and disruption of lymphatic drainage could be both responsible for these two cases. In this meta-analysis, post-embolization pain was only assessed in two studies, with low reported rates.

The damage of the gonadal artery during surgery may be a cause to post-operative scrotal pain linked to an interruption or reduction of blood supply to the testis. It is uncommon following LLDN, as gonadal artery is not dissected during the procedure, but gonadal artery wound could happen inadvertently and cause orchialgia no matter GV ligation level. To our knowledge, no cases were reported in the literature.

The damage of neural fibers of the spermatic plexus while clipping GV and ureter was another suggested hypothesis to explain post-operative orchialgia [11, 13]. Orchialgia may be due to sympathetic dystrophy after injury of the neural fibers leading to neuropathic pain. Kim et al. suggested to preserve gonadal vessels or to perform distal ligation to avoid disruption of neural tissue [11].

Shirodkar et al. suggested in 2011 a modified surgical procedure to avoid post-operative testicular pain in laparoscopic hand-assisted nephrectomy. The gonadal vein was spared, being ligated at the confluence of the renal vein. They reported no testicular pain, since they used modified procedure [15].

In 2015, Sureka et al. analyzed the impact of distal GV ligation on testicular symptoms occurrence for patients who underwent LLDN [15]. They prospectively randomized 40 patients whose GV ligation was above iliac vessel bifurcation and 30 patients whose GV ligation was below. Ipsilateral orchialgia was significantly more frequent in the “below” group versus the “above” group [9 patients (30%) versus 1 (2.5%) respectively, $p=0.001$]. In the same study, they also reported another group of 43 patients who underwent LLDN with GV ligation above iliac vessel bifurcation. In that group, no patient presented orchialgia. In our series, we reported a 26.1% rate of ipsilateral orchialgia following LLDN, despite distal ligation of the GV near the kidney lower pole, close to the renal vein confluence. These results put into question the mechanism of orchialgia, which may not be exclusively linked to GV ligation.

Regarding our findings, these following strategies could improve post-operative orchialgia management. GV distal ligation alone may not be sufficient. To prevent neural fibers damage, dissection of the tissue around GV should be avoided; if possible, preservation of GV may reduce pain related to neural and vascular damages, but has not been properly studied yet.

In case of post-operative testicular pain, patients should undergo physical examination. Doppler US could be performed according to pain characteristics and physical examination.

In this study, more than 70% of the patients managed their pain with no more than non-opioid analgesic (paracetamol) and the mean duration was 15 months. Only one patient was treated with medication for neuropathic pain. As neural cause would be difficult to exclude, it would be interesting to refer patients with unusual or long-lasting testicular pain (with normal clinical examination and Doppler US) to experts in chronic pain management who could evaluate neuropathic pain and prescribe specific treatment.

According to our results, our main suggestion would be to improve information given to patients. We modified our national urologic society information given to patients before LLDN to specify the risk of post-operative testicular events. Following surgery, they should be correctly advised to treat moderate pain with non-opioid analgesic (if needed) and to consult if they experience unusual pain such as acute, intense, or long-lasting pain or in case of analgesic inefficacy.

Considering the general male population, recent series reported chronic scrotal pain in 4.8% of men consulting an outpatient urologist [22]. Moreover, 25–50% of chronic orchialgia were classified as idiopathic [23]. In our study, we identified patients with testicular antecedents and could not find any correlation with post-operative testicular events: only one patient (4.1%) in the group with post-operative testicular events reported testicular antecedent as compared to 6 (13.3%) in the group free from post-operative testicular symptoms. These results suggest that post-operative orchialgia may be due to the surgery and not by any other general cause.

In our cohort, we reported 2 patients (9.1%) with contralateral orchialgia and 2 other patients (9.1%) with bilateral orchialgia. Among these patients, 1 had testicular antecedent of right epididymitis, and these symptoms could recur. Furthermore, we could not link this contralateral pain to another objective symptom. Finally, we cannot exclude the detection bias for these patients.

The mean delay of onset symptoms was 1 month in our study. To our knowledge, there are no evidences explaining this delay in the literature. One hypothesis could be the difficulty to discriminate pain's type and localisation in the early post-operative period. A second hypothesis could be donors' neglect of their symptoms in the context of organ donation. Finally, we cannot exclude a delay for the onset of orchialgia following vascular, lymphatic, or nervous post-operative disorder.

These results apply only for our donor population, it should be interesting to lead a similar study for male

patients who underwent nephrectomy for any cause, to generalize post-operative information.

The main limits of our study are the retrospective data collection including chart review and phone interview at least 1 year after surgery and the use of a non-validated questionnaire. Individual phone call could add detection bias and over-estimation of complaints rate. A validated questionnaire to assess social and professional impact of orchialgia could be of interest for further investigation. Moreover, our low size population is another limitation of this study.

Following our questionnaire, every patient mentioned having been correctly informed during the pre-LLDN consultation about the main risks and potential residual abdominal pain. However, no one was informed on possible post-operative orchialgia. No patient with post-operative orchialgia mentioned regrets regarding kidney donation. This study suggests the necessity to change our information about kidney donation. Patients should be informed about orchialgia during the pre-donation medical consultation.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Research involving human participants and/or animals Retrospective analysis, this research did not involve human participants and/or animals

Informed consent For this study, oral consent was obtained for every patient.

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