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ORIGINAL PAPER

Safety of percutaneous nephrolithotomy in patients on chronic anticoagulant or antiplatelet therapy

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Abstract

In developed countries, the incidence of cardiovascular disease is increasing, therefore, anticoagulant and antiplatelet drugs are a widespread treatment nowadays. Percutaneous nephrolithotomy (PNL) is the first-line treatment for large or complex stones (> 2 cm) and remains an alternative for the smaller ones. The objective of this study is to analyze whether PNL surgery is a safe procedure in patients under a treatment discontinuation protocol for anticoagulant or antiplatelet therapies. We retrospectively studied 301 patients who underwent PNL in our hospital between 2008 and 2016 and identified 46 patients on chronic antiplatelet or anticoagulation treatment. With respect to PNL outcomes, the stone-free rate was similar (78 vs 74%, $p = 0.762$) in both groups, without any significant differences in the overall postoperative complications (17 vs 26%, $p = 0.203$). The incidence of hemorrhagic complications was similar between groups (12 vs 9%, $p = 0.492$), as demonstrated by the mean drop in hemoglobin (Hb), which was comparable in both cohorts (2.2 ± 1.3 vs 2.0 ± 1.4 $p = 0.270$) and the blood transfusion rate (14% in group A and 8% in group B, $p = 0.205$). No thromboembolic events were found within the year after the PNL procedure. PNL is a safe and effective intervention in patients under a treatment discontinuation protocol for anticoagulant or antiplatelet therapies. Although our study demonstrates the feasibility of this protocol, new scientific evidence aims to stratify the thromboembolic and bleeding risk of each patient to individualize the perioperative management thereafter.

Keywords PNL · Percutaneous nephrolithotomy · Antiaggregation · Anticoagulation · Antiplatelet therapy · Hemorrhagic risk · Stone disease · Urolithiasis

Introduction

In developed countries, the incidence of cardiovascular disease is increasing [1], therefore, anticoagulant and antiplatelet drugs are a widespread treatment nowadays. In Spain, 17.5% of patients undergoing surgical interventions are on antiplatelet therapy [2] and the prevalence of atrial fibrillation, one of the main indications for anticoagulant therapy is 8.5% [3]. Stone disease is also on the rise. The incidence of urolithiasis in Germany was found to be 1.47% in 2000 compared to 0.54% in 1979, with similar rises in other western countries [4, 5]. Consequently, many patients with stone disease are on anticoagulant or antiplatelet therapies.

Percutaneous nephrolithotomy (PNL) is the first-line treatment for large or complex stones (> 2 cm) and remains an alternative for the smaller ones [6]. PNL has a moderate risk of hemorrhage, which may be increased if it is carried out on anticoagulant or antiplatelet treatment. A common practice in moderate or high hemorrhagic risk procedures is to withdraw the anticoagulant or antiplatelet therapy to lessen the likelihood of bleeding. However, this maneuver is not entirely free of risks, since treatment discontinuation might lead to thromboembolic complications.

The objective of this study is to analyze whether PNL surgery is a safe procedure in patients under a treatment discontinuation protocol for anticoagulant or antiplatelet therapies.

Materials and methods

We retrospectively studied 301 patients who underwent PNL in our hospital between 2008 and 2016. Percutaneous tracts carried out through a sheath smaller than 24 Charrière (Ch) were excluded, leaving 286 patients for analysis.

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We identified 46 patients on chronic antiplatelet or anticoagulation treatment. The majority of them were on antiplatelet treatment with acetylsalicylic acid 100 mg (32 patients), acetylsalicylic acid 300 mg (3 patients), clopidogrel (3 patients) or acetylsalicylic acid plus clopidogrel (3 patients). The remaining five were on anticoagulation with acenocoumarol (a vitamin K antagonist) for atrial fibrillation. Indications are specified in Table 1.

Following our protocol (Fig. 1), we discontinued anticoagulants 5 days before the intervention, bridging with low-molecular weight heparin (LMWH) and restarting treatment 10 days later. Antiplatelet therapy was stopped 7 days prior to and resumed 10 days after surgery. Following PNL, a low-dose LMWH was started for all the patients as thromboembolic prophylaxis.

Table 1 Patient indications for antiplatelet and anticoagulation treatment

Antiplatelet subgroup	*n*
Primary prevention	19
Ischemic cardiopathy	
Stable angina	4
Drug-eluting stent	4
Bare-metal stent	1
Prosthetic heart valve	1
Ischemic stroke	3
Vasculopathy	
Peripheral arterial disease	3
Aortic aneurysm	1
Antiphospholipid syndrome	1
Anticoagulation subgroup	***n***
Atrial fibrillation	5

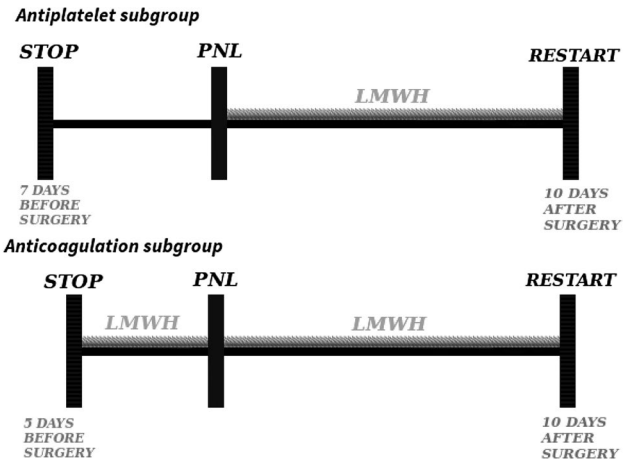

Fig. 1 Perioperative antiplatelet and anticoagulation discontinuation protocol in our center

In all cases, a blood test with coagulation parameters and a non-contrast CT scan was carried out prior to surgery and postoperatively. PNL was performed by the same surgeons in the Galdakao-modified Valdivia position [7]. Calyceal puncture was performed using a 16 Gauge needle and under ultrasound and X-ray guidance. Percutaneous tract was dilated using the semirigid Amplatz set or high pressure balloons, depending on the surgeons' preference. Rigid and flexible nephroscopes were systematically used. Several lithotripsy devices, such as pneumatic-ultrasonic and Holmium laser were available and used conveniently. No modifications in the technique were made during this period.

PNL safety was assessed by weighing the incidence of hemorrhagic complications and thromboembolic events in the first postoperative year between patients under chronic antiplatelet or anticoagulation treatment (group A) and those without any of these medications (group B).

Continuous variables are expressed in frequency and percentage, while the quantitative ones are expressed in mean ± standard deviation or median and interquartile range. Continuous data are compared using the *t* test if the distribution of samples was normal or Mann–Whitney *U* if the sample distribution was asymmetrical. Counts are compared by the Chi-square test. *P* values less than 0.05 are considered statistically significant. Statistical analysis was conducted using SPSS v.20.

Results

Patients were significantly older in group A (68 ± 10 years vs 55 ± 14, $p = 0.000$) and also had a higher score in the American Society of Anesthesiologist (ASA) physical status classification system (52 vs 17% of ASA ≥ 3, $p = 0.000$). No differences in the stone burden, its distribution and in prior SWL or surgery in the kidney were found between groups. International normalized ratio (INR) mean was less than 1 in both groups (0.97 ± 0.10 vs 0.97 ± 0.07, $p = 0.997$). Patient demographics and characteristics are listed in Table 2.

Tables 3 reflects that the PNL technique carried out in either group was not significantly different regarding the calyx of access, its caliber, the number of tracts, the method of dilation chosen, the operating time and drainage decision.

With respect to PNL outcomes (Table 4), the stone-free rate was similar (78 vs 74%, $p = 0.762$) in both groups, without any significant differences in the overall postoperative complications (17 vs 26%, $p = 0.203$). The incidence of hemorrhagic complications was similar between groups (12 vs 9%, $p = 0.492$), as demonstrated by the mean drop in hemoglobin (Hb), which was comparable in both cohorts (2.2 ± 1.3 vs 2.0 ± 1.4 $p = 0.270$) and the blood transfusion rate (14% in group A and 8% in group B, $p = 0.205$). No

Table 2 Patient demographics and characteristics depending on whether they were under antiplatelet or anticoagulation treatment (group A) or not (group B)

	Group A $n=42$	Group B $n=244$	p
Age, years	68 ± 10	55 ± 14	0.000
Female sex, *n* (%)	23 (55)	147 (60)	0.504
BMI, Kg/m^2	29.2 ± 4.5	28.4 ± 5.2	0.375
ASA score ≥ 3, *n* (%)	22 (52)	41 (17)	0.000
Stone burden, mm^2	398 [243, 864]	376 [236, 556]	0.417
Distribution			
Single	15 (36)	77 (32)	0.960
Multiple	5 (12)	40 (16)	
Staghorn	22 (52)	127 (52)	
Prior SWL or surgery, *n* (%)	21 (50)	123 (50)	0.961
Preoperative INR	0.970 ± 0,10	0.969 ± 0,07	0.997

BMI body mass index, *SWL* shock wave lithotripsy, *INR* international normalized ratio

Table 3 Intraoperative variables, depending on whether the patients were under antiplatelet or anticoagulation treatment (group A) or not (group B)

	Group A $n=42$	Group B $n=244$	p
Access calyx			0.881
Upper, *n* (%)	2 (5)	19 (8)	
Middle, *n* (%)	6 (14)	33 (14)	
Lower, *n* (%)	34 (81)	191 (78)	
Access caliber			0.655
24 Ch, *n* (%)	31 (74)	193 (79)	
30 Ch, *n* (%)	11 (26)	50 (21)	
Single access, *n* (%)	42 (100)	240 (98)	0.403
ECIRS, *n* (%)	9 (21)	58 (24)	0.741
Amplatz dilation, *n* (%)	37 (88)	220 (90)	0.682
Surgical time (min)	96 [66, 135]	100 [80, 142]	0.534
Drainage			
Double J stent, *n* (%)	15 (36)	78 (32)	0.936
Nephrostomy tube, *n* (%)	1 (2)	5 (2)	
Double J + nephrostomy, *n* (%)	26 (62)	160 (65.6)	
Tubeless-stentless, *n* (%)	0 (0)	1 (0.4)	

Ch Charrière, *ECIRS* endoscopic combined intrarenal surgery

thromboembolic events were found within the year after the PNL procedure.

Table 4 PNL outcomes, depending on whether the patients were under antiplatelet or anticoagulation treatment (group A) or not (group B)

	Group A $n=42$	Group B $n=244$	p
Stone-free rate, *n* (%)	32 (78)	172 (74)	0.762
Overall complications, *n* (%)	7 (17)	63 (26)	0.203
Hemorrhagic complications, *n* (%)	5 (12)	21 (9)	0.492
Mean hemoglobin fall, g/dL	2.2 ± 1.3	2.0 ± 1.4	0.270
Blood transfusion rate, *n* (%)	6 (14)	20 (8)	0.205
Thromboembolic event, *n* (%)	0 (0)	0 (0)	NA

NA not applicable

Discussion

Perioperative bleeding is a common complication in PNL, with reported transfusion rates ranging between 2 and 20% in the literature [7, 8]. Seitz et al., in a recent review of PNL complications, estimated a mean transfusion rate of 7% and a mean drop in hemoglobin of 2.3 g/dL. This risk of hemorrhage increases in larger tracts, multiple punctures, the advent of a renal pelvis perforation and low preoperative hemoglobin levels [9]. Besides, when the Amplatz sheath is removed at the end of the intervention, hemostasis relies on the activation, adhesion, and aggregation of platelets along with the deposition and maturation of fibrin. Therefore, treatments affecting this cascade such as antiplatelet and anticoagulant drugs are of particular concern, and consequently this surgery is contraindicated in the absence of normal clotting parameters.

In patients under chronic anticoagulation, the most common and classical approach before surgery is bridging therapy, without differences in outcomes between using unfractionated heparin (UFH) or LMWH [10, 11]. As described before we are currently using bridging therapy with LMWH, in agreement with European Association of Urology guidelines [6], as PNL is considered a high-risk bleeding procedure. It is clearly appropriate in high-risk indications such as prosthetic metallic heart valves [12, 13]. Nevertheless, in the atrial fibrillation scenario, new studies show that forgoing bridging anticoagulation was not inferior to perioperative bridging with LMWH for the prevention of arterial thromboembolism, with the benefit of lowering the risk of major bleeding [14]. Another open debate is the management of the new non-vitamin K antagonist oral anticoagulants (NAOCS), such as Dabigatran, Apixaban, Rivaroxaban and Edoxaban for patients undergoing elective surgery. A recent review on the periprocedural management of these patients seems to indicate that bridging therapy is not recommended should a discontinuation period for the NAOCS be required [15].

Antiplatelet treatment and its perioperative management remains controversial. Burger et al. [16] reported in their meta-analysis that patients on low-dose acetylsalicylic acid (AA) treatment had a 1.5-fold risk of postoperative bleeding, but neither did it increase the severity of the hemorrhagic complications nor the perioperative mortality due to them, except for neurosurgery and transurethral resection of the prostate. Concerning PNL, there is a lack of data regarding its safety without discontinuation of AA or other antiplatelet drugs. Kefer et al. [17] and Nerli et al. [18] published their PNL results using similar protocols of antiplatelet discontinuation therapy. Kefer et al. reported a 1.5 g/dL hemoglobin fall, 7% bleeding complications without any transfusion rate, and 4% thromboembolic complications. Similarly, Nerli et al. described a 1.6 g/dL drop in hemoglobin, 50% transfusion rate, without the advent of thromboembolic complications.

Therefore, undergoing PNL surgery under these treatments might lead to a higher risk of hemorrhagic complications. Conversely, treatment withdrawal may lead to cardiovascular events in some patients. However, the exact incidence of this complication is uncertain, with most of the data deriving from retrospective studies. Burger et al. [15] found that AA withdrawal preceded up to 10.2% of acute cardiovascular syndromes.

Patients with coronary stents are at the highest risk of suffering cardiovascular events when withdrawing these therapies. In these cases, PNL surgery should be postponed, if possible, for 4 weeks in bare-metal stents, and for 3 and 6 months in the Sirolimus-eluting and Paclitaxel-eluting ones, respectively [19]. Furthermore, since the highest risk of thrombosis appears within 7–15 days after antiplatelet therapy discontinuation, it is essential to restart treatment as soon as possible [10, 19].

In patients suffering from kidney stone disease and under anticoagulation or antiplatelet therapies at high risk of cardiovascular events, an alternative to PNL is to carry out a retrograde intrarenal surgery (RIRS). Kuo, Watterson and Turna published their respective series of RIRS in patients with not-reverted anticoagulation (INR ranging from 1.8 to 2.3), bleeding diastasis or antiplatelet therapy, with a low incidence of complications and stone-free rates ranging from 81.1–96% [20–22].

Limitations to our study, in addition to its retrospective design, might be that most of the patients in the antiplatelet group are on primary prevention, and therefore, their risk of thrombosis is low (i.e., comparing them to patients with coronary stents). The same shortcoming occurs in the anticoagulation group, bearing in mind that atrial fibrillation is one of the indications with less thromboembolic risk. However, a possible advantage of this study is that, despite being retrospective, the two cohorts are comparable in their demographic and technical characteristics, with the only exception of a higher ASA score and age in the antiplatelet/anticoagulant group, inevitably associated with patients having more comorbidities and, therefore, need preventive treatment of cardiovascular events. Finally, this is also a homogenous series, since no changes in the technique or the surgeons involved were made along the study period.

Conclusion

PNL is a safe and effective intervention in patients under a treatment discontinuation protocol for anticoagulant or antiplatelet therapies. Although our study demonstrates the feasibility of this protocol, new scientific evidence aims to stratify the thromboembolic and bleeding risk of each patient to individualize the perioperative management thereafter.

Author contributions CF-B: Protocol development, data collection, data analysis, manuscript writing. DAP-F: Protocol development, data collection, data analysis, manuscript writing. JFS: Data Collection. C García: Protocol Development.

Compliance with ethical standards

Conflict of interest DA Pérez-Fentes has financial relationship with Boston Scientific, Coloplast, Olympus, Cook, Presurgy, Palex. The rest of the authors declare that they have no conflict of interest.

Research involving Human Participants and/or Animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent for the technique was obtained from all individual participants included in the study.

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