

Intrarenal temperature measurement associated with holmium laser intracorporeal lithotripsy in an ex vivo model

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Introduction The aim of this article was to quantify the effect of the use of holmium laser during intracorporeal lithotripsy in an ex vivo model.

Material and methods A simulated model for laser nephro-lithotripsy was designed. Two ex vivo porcine kidneys were used. Electronic thermometer electrodes were inserted on the upper calyx. Intracorporeal lithotripsy was simulated with a holmium laser. Intrarenal temperature was recorded both at the beginning and after one minute of laser use with delta temperature (DT) defined as the difference between them. Measurements were made at different irrigation heights (30, 40, and 50 cm H₂O), frequency (Hz), and laser energy (J) in addition to the presence or absence of the access sheath. Analysis of factors associated with temperature change was performed.

Results Thirty-eight observations were recorded. The measurement without the use of access sheath showed an average DT of 4.9, 5.1, and 6.5°C for 5, 10, and 15 Hz, respectively; however, with a sheath, DTs were 0.2, 0.5, and 1.5°C. In terms of energy, mean DTs of 4.3, 6.1, 5.2, and 13.9°C for 0.5, 0.8, 1.0, and 1.5 J were recorded; in contrast, with a sheath, averages of 0.4, 0.5, 0.5, and 3.8°C, respectively were noted. In the adjusted model, energy, frequency, and use of sheath and water height were significant.

Conclusions The configuration of the laser significantly modifies the intrarenal temperature and height of the bladder irrigation. The use of an access sheath provides lower intrarenal temperatures regardless of laser configuration and water height.

Key Words: holmium ◊ urolithiasis ◊ temperature ◊ lithotripsy

INTRODUCTION

The holmium laser was introduced in the 1990s as a new option for treatment of kidney stones using intracorporeal lithotripsy and is the standard method for all types of kidney stone treatment [1, 2]. In contrast to short pulse lasers that cause fragmentation via photomechanical effects, the long pulse holmium laser produces fragmentation via both photomechanical effects and chemical decomposition [3]. Advances in laser technology and development of high-power lasers have allowed the development of new techniques, such as the dusting technique, for kidney stones comminution [4, 5]. This technique

uses high-energy settings that can reach 40 W with pulse energies between 0.2 and 0.5 J and high frequency up to 80 Hz. At higher powers, greater energy production with a higher risk of producing thermal injury in tissues occurs [6].

It is known from the thermal ablation literature that temperature and maintained ablation time are factors that contribute to cell death [5]. Previous studies have reported that the elevation of kidney temperature is produced with 20 and at 40 W [6]. Saporato et al. showed that a temperature of 43°C for 120 min is lethal for tissues; thus, for higher temperatures less time would be required for the same effect. Likewise, a rapid increase in temperature at the beginning

of laser lithotripsy can expose the tissue to harmful high temperatures, which can damage the collecting system and the ureter [7, 8].

Active measures for reducing heat production and limiting cell damage include intermittent laser activation during the procedure, stopping at 10 sec of activation, decreasing the temperature enough to avoid dangerous levels, and achieving a reduction in fluid temperature inside the kidney [6]. Another technique consists of maintaining adequate irrigation during ureteroscopy (URS) by using an access sheath that improves irritant outflow and decreases the intrarenal pressure [9, 10].

Few studies have established how the different variables to be regulated influence laser lithotripsy, such as time, energy, frequency, and flow. The study of Wollin et al. [11] is one of the few to examine the different variables through an *in vitro* model. This work is one of the first, if not the first, that analyzed how these variables affect renal temperature by comparing the presence or absence of an access sheath in *ex vivo* models. Our aim is to establish how different holmium laser settings, irrigation and the use of access sheaths produce intrarenal temperature changes.

MATERIAL AND METHODS

A model of intracorporeal lithotripsy was established to evaluate the intrarenal temperature *ex vivo* at the beginning and after one minute of laser use while regulating the irrigation pressure by modifying its height, frequency, and laser power during each measurement with or without ureteral access sheath.

Two *ex vivo* porcine kidneys were cold-preserved after the extraction, thawed on the same day of the experiment, and kept at room temperature during the procedure. Intracorporeal lithotripsy was simulated using a disposable flexible ureteroscope PUSEN 9.5 Fr diameter and the Holmium:yttrium/aluminum/garnet (Ho:YAG) laser with a 275 μm fiber trough as the working channel, placing it in the renal pelvic lumen and always activating it in the same position. No human samples were used.

To perform temperature measurements, both kidneys were punctured in the upper calyx (place where temperature was taken) and trough of the dilated path, and digital thermometer electrodes (DROK) were introduced the capability of measuring temperatures between -55 and 125°C . The laser was activated for 60 sec, and the intrarenal temperature was recorded both at the beginning and after one minute of laser use with Delta temperature (DT) as the difference between these two points, because the different initial temperature of the kidneys in the procedures.

Measurements were made at different irrigation heights (30, 40, and 50 cm H_2O , which corresponded to a flow of 8.5, 9.5, and 11.1 mL/min, respectively, frequencies of 5, 10, and 15 Hz, respectively, and energies of 0.5, 0.8, 1, and 1.5 J, respectively, with and without the ureteral access sheath (both conditions were exposed to the same parameters) after measuring basal temperature before each measurement. During the URS, saline solution was used at room temperature (Figures 1 and 2).

In the measurements obtained with ureteral access sheath, a 12/14 Fr sheath was used, which was ascended through the ureter to a distance of 1 cm from the pyeloureteral union.

Finally, descriptive and analytical statistics were performed, expressing the numerical variables as measures of central tendencies and the categorical variables as percentages. Analytical statistics were performed with the SPSS 22.0 software with a unimultivariate analysis using the covariance analysis (ANCOVA) model with a stepwise method in front of the dependent variable DT. P values <0.05 were considered significant. Joules, hertz, use of a sheath, and water height were considered co-variables after adjusting the model with the basal temperature variable. Analysis of variance (ANOVA) was used for paired samples in continuous variables (given the normal distribution of the continuous variable, according to the Shapiro–Wilk) and Bonferroni/Duncan tests for multiple comparisons.

RESULTS

Thirty-eight observations were recorded, each one with basal and one-minute temperature (Tables 1A and 1B). An irrigation pressure of 50 cm H_2O was determined to provide a flow of 11.1 cc/min, while 30 cm H_2O yielded a flow of 8.5 cc/min.

Irrigation height was founded to be significant in the DT determination in which a height of 50 cm H_2O decreased the DT by 4.8°C compared to 30 cm H_2O independent of the use of access sheath and laser configuration (Tables 1 and 2). For example, in the absence of an access sheath with a configuration of 0.5 J/15 Hz and using an irrigation of 30 and 50 cm H_2O , the delta temperatures obtained were 9.3 and 4.9°C , respectively, while when comparing both irrigation heights with a setting of 1J/15H, DT of 10.1 and 5.8°C were reached, respectively.

Regarding the frequency (Hz) with a configuration of 5, 10, and 15 Hz, average DTs without the use of ureteral access sheath of 4.9 , 5.1 , and 6.5°C , respectively, were observed, while with an access sheath, these values were 0.2 , 0.5 , and 1.5°C , respectively (Figure 3A). As an example, without the use

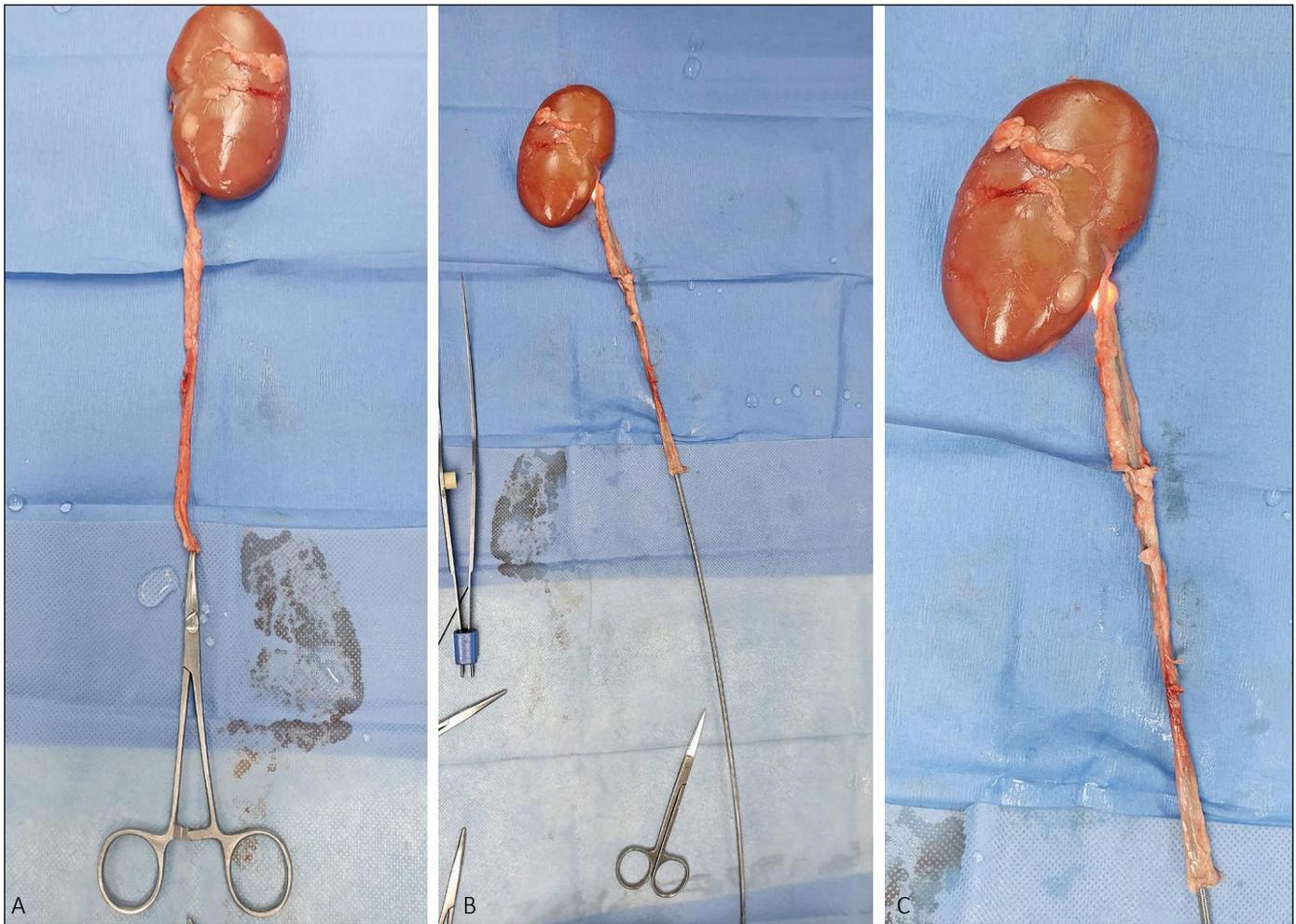


Figure 1. Ex-vivo model of porcine kidney prior to intracorporeal lithotripsy procedure (A). Access with flexible ureteroscope without use of access sheath (B). Kidney undergoing Ho:YAG laser activation (C).

of an access sheath and with an irrigation height of 50 cm H₂O, an energy of 1 J and a frequency of 5 and 15 Hz, the delta temperatures obtained per minute were 2.1 and 5.8°C, respectively.

In relation to energy (J), with a configuration of 0.5, 0.8, 1.0, and 1.5 J without using the access sheath, average DTs of 4.3, 6.1, 5.2, and 13.9°C, respectively, were recorded and when using access sheath, the averages were 0.4, 0.5, 0.5, and 3.8°C, respectively

Table 1. Multivariate analysis effect test

Model variables	p-value
Energy (J)	<0.001
Frequency (Hz)	0.048
Use of access sheath	<0.001
Height of the bladder irrigation (cm H ₂ O)	<0.001
Basal temperature (°C)	0.569

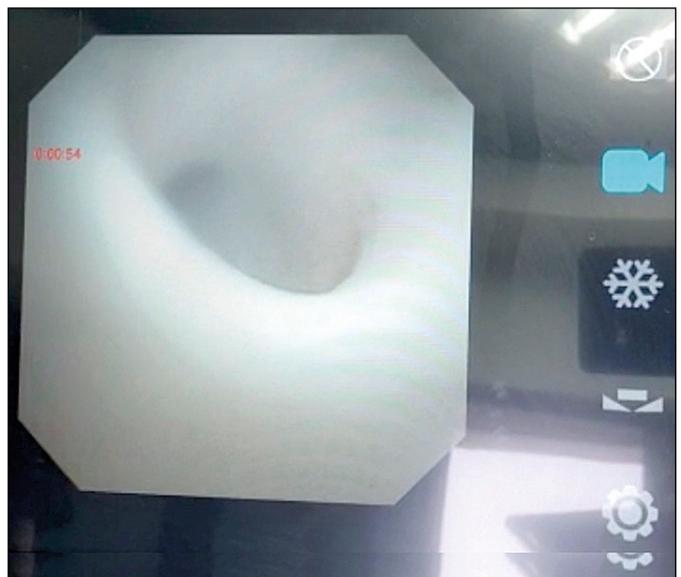


Figure 2. Endoscopic view of ex-vivo porcine kidney model through PUSEN flexible ureteroscope.

Table 1A. Temperatures recorded without ureteral access sheath

Kidney without ureteral access sheath									
Water height	Laser setting	Basal temperature (°C)	Temperature after 1 min (°C)	Laser setting	Basal temperature (°C)	Temperature after 1 min (°C)	Laser setting	Basal temperature (°C)	Temperature after 1 min (°C)
30 cm (flow: 8.5 cc/min)	0.5J–5 Hz	17.1	23	0.5J–10 Hz	22.1	28	0.5J–15 Hz	21.4	30.7
	0.8J–5 Hz	17	24	0.8J–10 Hz	19.7	32.1	0.8J–15 Hz	20	34
	1J–5 Hz	18.3	27.4	1J–10 Hz	22.5	33.5	1J–15 Hz	22.4	32.5
	1.5J–5 Hz	18.5	32.4						
40 cm (flow: 9.5 cc/min)	0.5J–5 Hz	16.6	17.2	0.5J–10 Hz	16.6	18	0.5J–15 Hz	17.3	19.5
	0.8J–5 Hz	18.3	19	0.8J–10 Hz	18.3	20.6	0.8J–15 Hz	17.7	20.6
	1 J–5Hz	18.3	19	1 J–10 Hz	18	19.4	1 J–15 Hz	18.4	20.3
50 cm (flow: 11.1 cc/min)	0.5J–5 Hz	23	28.8	0.5 J–10 Hz	22.6	23.3	0.5 J–15 Hz	22.5	27.4
	0.8 J–5 Hz	21.5	25.2	0.8 J–10 Hz	22.5	27.3	0.8 J–15 Hz	22.1	29.6
	1 J–5 Hz	23	25.1	1 J–10 Hz	22.3	26.7	1 J–15 Hz	22.4	28.2

Table 1B. Temperatures recorded with ureteral access sheath

Kidney with ureteral access sheath									
Water height	Laser setting	Basal temperature (°C)	Temperature after 1 min (°C)	Laser setting	Basal temperature (°C)	Temperature after 1 min (°C)	Laser setting	Basal temperature (°C)	Temperature after 1 min (°C)
30 cm (flow: 8.5 cc/min)	0.5 J–5 Hz	20.4	20.3	0.5 J–10 Hz	20.1	20.3	0.5 J–15 Hz	20	21.1
	0.8 J–5 Hz	20.3	20.8	0.8 J–10 Hz	20.5	20.9	0.8 J–15 Hz	21.1	21.6
	1 J–5 Hz	21.4	21.6	1 J–10 Hz	21.1	21.9	1 J–15 Hz	21.3	21.
50 cm (flow: 11.1 cc/min)	1.5 J–15 Hz	21.5	25.3						

Table 2. Uni-multivariate analysis of delta temperature (DT) associated factors. Basal temperature is used as the adjustment variable

Variables	Univariate Coefficient [95% CI]	p-value	Multivariate Coefficient [95% CI]	p-value
Energy (Joules):				
0.5 J	-5.5 [-11.8 – 0.8]	0.045	-7.0 [-9.4 – -4.7]	<0.0001
0.8 J	-4.1 [-10.4 – 2.2]	0.194	-5.6 [-7.9 – -3.3]	<0.0001
1.0 J	-4.8 [-11.1 – 1.5]	0.129	-6.4 [-8.9 – -3.9]	<0.0001
1.5 J	0*	–	0*	–
Frequency (Hertz):				
5 Hz	-1.1 [-4.4 – 2.2]	0.500	-2.1 [-3.3 – -0.8]	0.002
10 Hz	-0.9 [-4.3 – 2.4]	0.556	-1.1 [-2.3 – 0.03]	0.056
15 Hz	0*	–	0*	–
Height of the bladder irrigation (cmH₂O):				
30 cmH ₂ O	0.9 [-2.7 – 4.4]	0.621	4.8 [3.1 – 6.5]	<0.0001
40 cmH ₂ O	0.5 [-1.7 – 2.6]	0.559	2.7 [0.5 – 5.4]	0.046
50 cmH ₂ O	0*	–	0*	–
Use of access sheath:				
No	4.7 [2.1 – 7.4]	0.001	8.8 [7.5 – 10.1]	<0.0001
Yes	0*	–	0*	–
Basal temperature (°C)	-0.5 [-1.5 – 0.5]	0.321	0.09 [-0.4 – 0.6]	0.710

(Figure 3B). As an example, without using an access sheath with an irrigation height of 30 cm H₂O, a frequency of 5 Hz and an energy of 0.5 and 1.5 J, the resulting delta temperatures were 5.9 and 13.9°C, respectively.

Finally, in the adjusted multivariate model, both the energy (J), frequency (Hz), use of access sheath, and water height were significant (Tables 1 and 2) in which the variation of DT for 1.5 J was 7.0°C greater than for 0.5 J (while the rest of the settings remained constant), whereas in the case of the frequency, a configuration of 15 Hz caused an increase in DT by 2.1°C compared to 5 Hz. The use of an access sheath versus no sheath caused a decrease in the DT by 8.8°C (adjusted by the other variables) and an irrigation height of 50 cm H₂O decreased by 4.8°C in relation to 30 cm H₂O. The basal temperature was not significant in the model; however, it was included in the model as it was the adjustment variable.

DISCUSSION

The holmium laser is the standard method for intracorporeal lithotripsy of all kidney stone types [1,2]. However, even though it is considered one of the most safe lasers in endourology [2], its use is not free

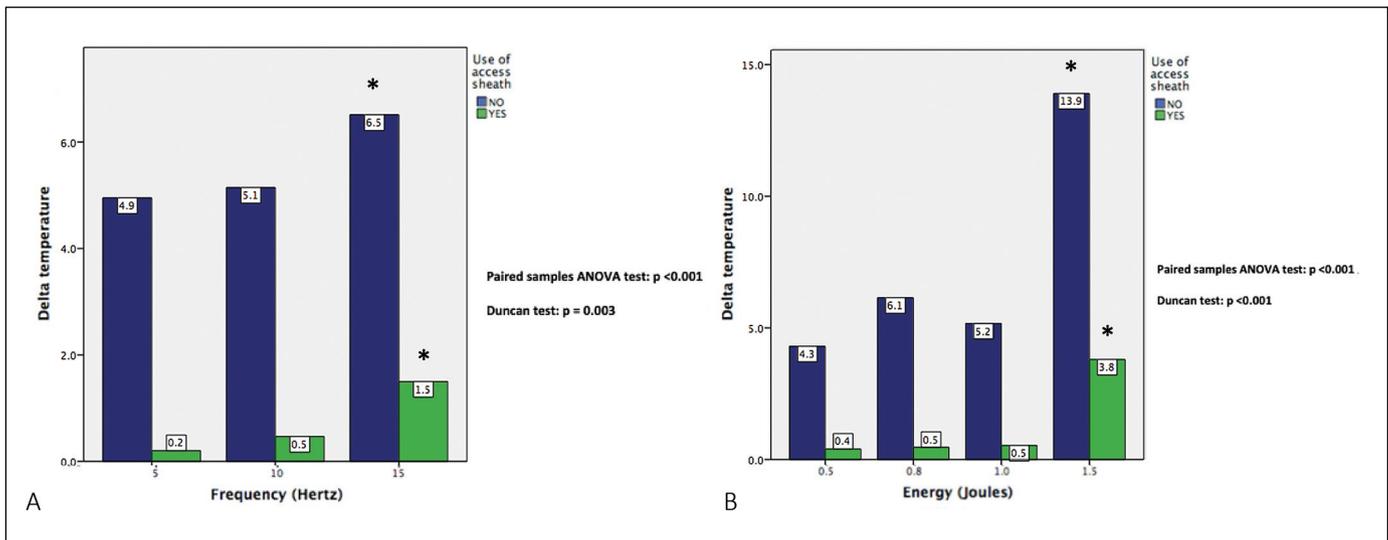


Figure 3. Delta temperature (DT) average according to frequency (A) and energy (B), grouped by use of ureteral access sheaths. A uni-variaded tendency is shown in different levels of qualitative variable.

*Significant level according to multiple comparison test (Duncan)

of risk or complications. These risks include mechanical trauma and direct thermal damage to tissues. It has been shown that at a distance of 0.5 mm and a power of 5 W (0.5 J/10 Hz), the use of Ho:YAG laser produces ureteral perforation after 2 sec in ex-vivo porcine models [3]. Through its photothermal effect, an increase in tissue temperature occurs, reaching values above 43°C, which are exponentially associated with cellular cytotoxicity [4]. To prevent injuries secondary to the use of lasers in this context, it is necessary to establish which variables determine a thermal rise in tissues since few studies to date exist. Our study is one of the first to analyze how intrarenal temperature is affected by various parameters, such as flow and laser configuration (frequency and power) and at the same time, it compares the presence or absence of ureteral access sheath in the ex vivo model.

The use of ureteral access sheath (UAS) is associated with an increase in irrigation flow during flexible URS by establishing a continuous outflow and potentially, reducing operatory times [5, 6]. A systematic review in 2018 that included 83 articles, showed that there was no evidence to support that its use has a cooling effect on the surrounding tissue by increasing the irrigation outflow exists [6]. However, a recently published study at the University of Patras (Greece) evaluated the effect of the use of an access sheath on the temperature of the irrigation fluid during the use of holmium laser in an in vivo porcine model, demonstrating that without the access sheath use, an increase in temperature in irrigation fluids at continuous flow and pressure occurred

[7]. These results are consistent with our study in which the use of access sheath provided a less steep increase in intrarenal temperatures after one minute of laser activation regardless of the configuration of the laser and height of selected irrigation with a decreased in DT at 8.8°C compared to measurements made in the absence of a sheath. This finding can be explained based on the increase in flow that occurs because of sheath installation, managing to maintain optimal irrigation levels that allowed convection and heat dissipation during the procedure. When evaluating the intrarenal and ureteral temperature, the time-temperature relationship must be considered, since 1°C above 43°C produces the same amount of cellular damage in half the time [10]; therefore, a decrease in flow can produce a rapid increase in temperature with consequent tissue damage, highlighting the importance of maintaining continuous irrigation flow (both inlet and outlet) throughout the procedure. Similarly, Molina et al. simulated lithotripsy with an Ho:YAG laser at a power of 10 W (1J/10Hz) for 3 sec using a fiber of 365 μm with and without the use of saline solution at 8 cc/seg (480 cc/min) in sheep ureters ex vivo. Tissue temperatures were significantly lower with the use of irrigation (37.4 \pm 2.5°C versus 49.5 \pm 2.3°C). However, we must emphasize that although the influence of the use of irrigation on the temperature profile was demonstrated in this study, the laser activation time and amount of flow used during irrigation are outside the parameters used in clinical practice [8].

Subsequently, Wollin et al. [4] evaluated the effects of different laser settings and irrigation flow on in-

traurethral temperature during lithotripsy using ureteroscopy with a Ho:YAG laser in an in vitro model. The maximum temperature without irrigation was above 100°C at 1 J/20 Hz, while in the rest of the settings, all temperatures were above 43°C. On the other hand, with flow rates of 50 and 100 cc/min only at 1 J/20 Hz, significantly higher values were achieved (43.5 and 30.7°C, respectively) thus demonstrating that without the use of irrigation, low power settings produce thermal increases that can potentially induce thermal damage to the ureteral tissue, while with an adequate flow, it is possible to maintain safe temperatures within an in vitro ureteral system [4]. These results are also consistent with our study in which the irrigation height turned out to be significant in the determination of the delta temperature. A height of 50 cm H₂O was associated with a greater flow than at lower heights and a decreased in DT by 4.8°C compared to 30 cm H₂O regardless of access sheath use and laser configuration. Among the various parameters that can be regulated in the lithotripter is the laser power (W), which determines the amount of energy it provides in each pulse that in turn depends on both the frequency and the energy [1, 9]. Both works of Wollin et al. used in vitro models, such as the one carried out at the University of Patras with in vivo porcine models, have shown that at higher power there is a greater thermal rise after the laser pulse both in the irrigation solution and in the ureteral tissue [4, 7]. However, it has not yet been established exactly to what extent the power and frequency used independent of each other affect the temperature. It is at this point that our model determined that both variables are significant in which the DT for 1.5 J was 7.0°C greater than for 0.5 J while in the case of the frequency a configuration of 15 Hz increases the DT by 2.1°C compared to one at 5 Hz. In this sense, our results allow us to estimate in a more concrete way how each parameter influences and thus establishes a margin of safety in clinical practice.

Finally, we must mention the study limitations. When evaluating tissue temperature, the penetration of photons into the tissue depends on the wavelength, which is determined by its structure [9]. When using a porcine model, there is a difference in the composition and fat distribution of renal/ureteral tissue with respect to human tissues. This difference may affect the final intrarenal temperature; in addition, the contribution of heat made by blood vessels in an in vivo model should be considered

as a determinant of temperature. Regarding the number of observations made (n = 38), we should mention that although we could obtain a greater quantity, the purpose of this study was exploratory, and sought to develop an initial analysis. Furthermore, it should be considered that human stones were not used in our simulation, so the effect of lithotripsy on intrarenal temperature may be overestimated. The holmium laser works through a photothermic mechanism, producing a direct absorption of its energy by the stone, which reduces the amount of energy that is dissipated to the tissues and in turn the intrarenal temperature. However, the amount of energy absorbed by each stone depends on its composition, especially on the amount of water molecules whose absorption peak is similar to the wavelength of the Ho:YAG laser [2].

Another parameter to consider is the use of irrigation solution at room temperature and not at different temperatures, losing the possibility of analyzing this effect. However, the basal temperature at which the experiment was carried out was not significant when performing the multivariate analysis, which was one of the reasons for including it as a covariate. The latter is not less since the lack of significance of the basal temperature can lead us to infer that the irrigation temperature may not be significant over the delta temperature when adjusting for the other variables. This point is also consistent with other studies in which with irrigation at 50 cm H₂O at room temperature (24.5°C) and body temperature (36.5°C), a Ho:YAG laser was fine for 5 min using different settings (0.5 J/20 Hz, 1 J/10 Hz, 2-3-4 J/Hz) with no differences in temperature increase after 1 min of laser activation [11].

CONCLUSIONS

In ex vivo kidneys, the laser configuration significantly modifies the intrarenal temperature and the flow determined by the irrigation height. The use of an access sheath provides lower intrarenal temperatures, independent of the laser configuration and the height of the irrigation, and was probably determined by the greater flow associated with its use. In this sense, our results open the door for the development of more studies in in vivo models that would allow us to confirm our findings.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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