

Risk factors associated with renal parenchymal fracture during laparoscopic cryoablation

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OBJECTIVE

To assess the risk factors for haemorrhage and renal fracture associated with renal cryoablation.

MATERIALS AND METHODS

In a porcine model, 120 cryoablations were administered in 26 pigs, with five groups of 24 ice-balls each; in groups 1 and 2 asynchronous cryoprobe activation was evaluated for the 1.47- and 3.4-mm cryoprobes (IceRods, Galil Medical, Plymouth Meeting, PA, USA), respectively; in group 3, three-3.4 mm cryoprobes were used to examine synchronous probe activation; in group 4 the 1.47-mm cryoprobe was used

to examine single-probe activation with premature cryoprobe extraction; and in group 5 we used a new 'guillotine' technique for upper-pole renal cryoablation. Ice-ball fractures and haemorrhage were characterized by the location, length and depth of each fracture, as well as the degree of bleeding.

RESULTS

In all, 26 domestic pigs successfully had renal cryoablation procedures. In group 1 and 4 there were no episodes of renal fracture; in group 2 renal fracture occurred in 10 (42%) trials. Group 3 had 22 (92%) renal fractures during the freeze/thaw cycle. Group 5 had 13 (54%) renal fractures during

the freeze/thaw cycle, and there was an additional ice-ball fracture during probe removal once in 24 times.

CONCLUSIONS

Renal fracture is most common with the application of larger 3.4-mm cryoprobes in the synchronous and asynchronous setting. Under standard application, smaller (1.47-mm) cryoprobes result in little renal fracture or bleeding. The use of the guillotine technique is associated with a greater risk of renal fracture.

KEYWORDS

cryoablation, renal, fracture, complications

INTRODUCTION

The application of ablative technologies for small renal cortical neoplasms continues to expand as a viable treatment option, due to the decreased morbidity associated with surgical ablation. Cryoablation is one of the most commonly used methods, as it is effective in producing complete tissue ablation, can be precisely targeted using imaging methods, and has the greatest follow-up of any ablative technology [1,2].

Although significant haemorrhage is rare with renal cryoablation using contemporary technology, renal fracture and bleeding occasionally occur during the procedure. In the larger series of renal cryoablation, the reported incidence of significant ice-ball fracture is 0–8.1% [3–5]. Blood transfusion rates of 1.8–2.7% have been reported [3–5].

To our knowledge, there has been no investigation to establish which factors are responsible for renal ice-ball fracture.

In our experience, we noted that renal fracture appears to be more common with asynchronous firing of cryoablation probes (initiating a second ice-ball after a primary ice-ball has started to form), premature extraction of probes (before complete thawing of the probe/ice-ball interface), or with ablations of upper pole renal lesions using the 'guillotine' technique. As such, we evaluated factors that might contribute to renal parenchymal fracture during cryoablation in a porcine model.

MATERIALS AND METHODS

The investigation was approved by our Institutional Animal Care and Use Committee. Power calculations were not done to obtain a sample size, as the study was a pilot. In all, 26 domestic pigs were divided into five groups. Groups 1 and 2 (six pigs each) were used to evaluate asynchronous (initiating different ice-balls next to each other at different times) ice-ball formation using the 1.47-mm

cryoprobes (IceRods, Galil Medical, Plymouth Meeting, PA) and the larger 3.4-mm cryoprobes, respectively. In group 3 we evaluated synchronous probe activation with the larger 3.4 mm cryoprobes. Groups 4 (two pigs) and 5 (six pigs) were used to evaluate premature probe removal and polar ablation or the 'guillotine technique' (Fig. 1), respectively.

Female domestic pigs (≈35 kg) were housed in the animal-care facility for 2 days to become acclimated. A pre-anaesthetic dose of ketamine HCl 5–10 mg/kg i.m. was administered and anaesthesia was maintained with isoflurane (1–5%) and oxygen (2–4 L/min) throughout the procedure. The pigs were initially placed prone; pneumoperitoneum was established through a Veress needle placed at the umbilicus. Once the intra-abdominal pressure reached 15 mmHg, the Veress needle was removed and a 12-mm trocar was placed at the umbilicus. The pigs were then placed in the flank position and secured to the

operating table. Two additional trocars were placed, one inferior to the umbilicus and lateral to the rectus abdominus muscles. The other was placed superior to the umbilicus and lateral to the rectus abdominus muscles. The kidney was identified, and the parietal peritoneum was removed, exposing the capsular surface of the kidney. The renal hilum was then dissected to gain control of the renal vasculature, if needed. All cryoprobes were placed percutaneously. Depending on the group, probe placement was as follows: in groups 1, 2 and 3, we evaluated renal fracture with synchronous (simultaneous) and asynchronous (adjacent ice-balls initiated at different times) activation of cryoablation probes with small (1.47 mm, group 1) and larger (3.4 mm, groups 2 and 3) cryoprobes, respectively. For groups 1, 2, and 3, a template was placed on the skin, and the probes were placed parallel to each other. The template consisted of an equilateral triangular configuration with probe separation at 2.0 cm. For groups 1 and 2, a template was used to guide the cryoablation probes in a standard fashion. To simulate asynchronous probe activation in the small porcine kidney, two probes were used to create the initial cryolesion, followed by insertion and activation of the third cryoprobe. Two probes were inserted into the intrapolar region of the kidney to a depth of 2 cm. The two probes were activated synchronously, and two 8-minute freeze cycles with an intervening active thaw cycle (3 min) were administered. After terminating the second freeze cycle, the probes were removed in the standard fashion by applying active thaw cycles until the probes were released freely from the tissue. With the existing ice-ball still intact, the third probe was inserted into the kidney just lateral to the edge of the existing ice-ball. The probe was then deployed (asynchronous firing) adjacent to the thawing ice-ball and followed the same freeze-thaw cycle of the two previous probes. At the end of both freeze cycles, the probe was removed in the standard manner. The procedure was repeated on the upper pole of the same kidney, as well as the upper and lower poles of the contralateral kidney for a total of 4 cryolesions per pig. For group 3 the same template was used, but three 3.4-mm probes were synchronously activated. Each ablation was monitored for ≥ 10 min after ablation. Any cracking of the ice-ball or renal surface, or bleeding, was documented and recorded in detail. Variables recorded included crack depth (0, none; 1, minimal; 2, moderate; and 3, severe), length

Mean variable	Group				
	1	2	3	4	5
No. of fractures	0	10	22	0	14
Severity of fracture	–	1.9	1.8	–	1.9
Length of fracture, mm	–	16.7	25	–	20.8
Severity of bleeding	–	1.3	1.8	–	0.9

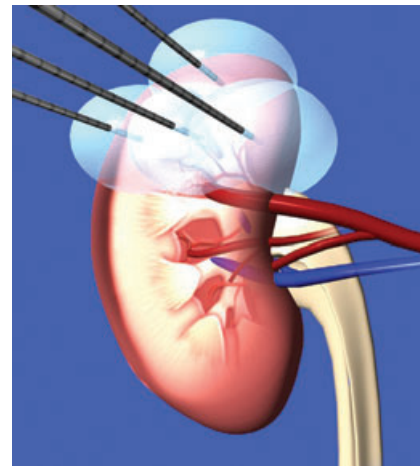
TABLE 1
The fracture rates for the different groups

of the fracture, location of the fracture (ice-ball or adjacent renal parenchyma), and severity of bleeding (0, none; 1, minimal; 2, moderate; and 3, severe). Significant bleeding was controlled with Floseal (Baxter Bioscience, Deerfield, IL, USA) and pressure, as needed.

In group 4 the effects of premature probe extraction were evaluated. Two pigs had 24 ablations with a single probe per kidney, for a total of 24 lesions. One 1.47-mm probe was inserted percutaneously in the lower pole and two 8-min freeze cycles, with a 3-minute intervening active thaw cycle, were administered. On completing the final freeze cycle the probe was immediately rotated while simultaneously activating the thaw cycle. Each probe defect was monitored for bleeding 10 min after probe removal. The procedure was repeated six times in each kidney for a total of 12 observations per pig.

Pigs in group 5 were used to evaluate ice-ball and parenchymal bleeding with an upper-pole ablation technique (guillotine; Fig. 1). This technique, which we have used clinically for upper-pole tumours at the most cephalad portion of the kidney, involves passage of cryoablation probes through the upper pole, and deployment of an additional probe in the upper-pole tumour. Three 1.47-mm cryoprobes were placed transversely along the mid/upper pole junction at a spacing of 1.5 cm. The three probes were deployed in a 'through-and-through' manner such that the tip of the probe was seen extending outside of the posterior aspect of the kidney. The fourth probe was placed at 2 cm from the middle guillotine probe into the upper pole (Fig. 1). A double 8-min freeze with an intervening 3-minute active thaw was administered. At the end of the last thaw cycle the probes were removed in the standard manner. This cycle was repeated in the lower pole of the same kidney and the upper and lower poles of the contralateral kidney for a total of four cryolesions per pig. Each guillotine cryolesion

FIG. 1. The guillotine technique.



was monitored for 10 min after ablation. All results were assessed using descriptive statistics, as the mean (SD) and range.

RESULTS

All 24 pigs successfully had laparoscopic renal cryoablation, with 24 cryolesions created per group, for 120 cryolesions in all; the results of all trials are summarized in Table 1. Pigs in group 1 and 4 had no evidence of renal fracture during the freeze/thaw cycles or during probe removal. In group 2, during asynchronous activation of 3.4 mm probes, there was renal fracture during the freeze/thaw cycles in 10 (42%) of the trials. Of the 10 renal fractures, five were in the upper pole and another five in the lower pole of the kidney. The mean fracture severity score was 1.9 (0–3), the mean size of the renal fracture 16.7 (2–25) mm and the mean severity of bleeding score from the renal fracture was 1.3 (0–3).

In group 3, there were 22 (92%) fracture events during the freeze/thaw cycles, of which 12 were in the upper pole and 10 in the lower pole of the kidney. The mean fracture severity score was 1.8 (1–3), mean size of the

renal fracture 25.0 (3–45) mm, and the mean severity of bleeding from the renal fracture 1.8 (0–3). There were no fractures as a result of probe extraction.

In group 5, there were 14 (58%) fractures, of which 13 (54%) were during the freeze/thaw cycles and one (4%) was during probe removal. Of the 13 renal fractures in group 5 (guillotine technique), six were in the upper pole and seven in the lower pole of the kidney. The mean fracture severity score was 1.9 (0–3), the mean size of the renal fracture 20.8 (0–40) mm and the mean severity score of bleeding from the renal fracture 0.9 (0–3). In group 5, the one fracture as a result of cryoprobe extraction resulted in a 20-cm crack in an upper pole kidney, and resulted in severe bleeding.

DISCUSSION

One of the major advantages of renal cryoablation over extirpative approaches such as open or laparoscopic partial nephrectomy is the decreased morbidity that is associated with the procedure. Renal parenchymal or ice-ball fracture during cryoablation procedures are rare events, but represent a fair proportion of the complications associated with renal cryoablation. In our clinical experience, significant ice-ball fracture with bleeding requiring transfusion has an incidence of $\approx 3\%$ [6]. However, we noted that bleeding is more common under certain circumstances. This study was designed to evaluate different cryoablation conditions to optimize haemostasis during renal cryoablation.

The standard double freeze–thaw cycle used in the present study is the same as that described by Woolley *et al.* [7]. Cryoprobes were placed as described by Weld *et al.* [7,8] as the standard method for cryoprobe targeting. The investigational techniques studied several deviations from the standard technique, such as asynchronous probe activation (creation of ice-balls that are not initiated at the same time), and a modified probe configuration that we have used clinically to ablate upper pole renal cortical neoplasms, known as a 'guillotine technique'. This study provides clinically relevant data on the risk factors for renal bleeding and renal fracture as a result of cryoablation.

For the 1.47-mm cryoprobes, extraction before completing the 1-min thaw cycle did

not result in renal fracture or additional bleeding from the probe defect. Despite the counterintuitive data, care should always be used during probe extraction. While clinically premature extraction of cryoablation probes is associated with ice-ball fracture, it is likely that we did not have ice-ball fracture in this setting as we used only one 1.47-mm probe. It is likely that applying larger probes or multiple smaller probes would have resulted in bleeding during premature probe extraction.

Asynchronous ice-ball creation was tested as this is a useful clinical technique during renal cryoablation procedures when the surgeon believes that a section of the targeted renal neoplasm has not been adequately engulfed by the ice-ball. In this setting, it is feasible to add another cryoablation probe to the area that has been inadequately treated for a complete and successful ablation.

In evaluating asynchronous probe deployment we noted that the larger 3.4-mm cryoprobes placed in a standard triangular configuration while being asynchronously activated caused renal fracture 42% of the time during the freezing/thaw process. The current data support the practice of asynchronous ice-ball creation with smaller (1.47 mm) probes. Conversely, when using larger probes, surgeons should consider waiting for the primary ice-ball to melt completely before deploying an additional probe(s).

As the 3.4-mm and the 1.47-mm probes have been shown to produce ice-balls and areas of complete ablation that are similar in volume [9], it seems likely that the cause of the renal parenchymal fracture and bleeding was mechanical trauma to the tissue and ice-ball from the larger cryoablation probes. Mechanical trauma, rather than intrinsic ice-ball fractures, as a source of bleeding in this setting is supported by our laboratory experience with the larger 3.4-mm cryoprobes. The larger probes commonly resulted in some form of parenchymal fracture.

We also tested the 'guillotine technique' that we developed for the laparoscopic treatment of renal cortical neoplasms located at the most cephalad portion of the kidney. We strongly feel that optimum targeting of renal cortical neoplasms, no matter which energy method is used for ablation, is achieved by deploying one or several probes placed

perpendicular to the surface of the tumour/kidney. Even with maximum mobilization of the kidney, perpendicular probe placement into a very cephalad renal mass is not feasible. As such, the 'guillotine' technique is used to ablate the entire upper pole, including the target renal lesion and a margin of normal renal parenchyma. The current study confirms that the guillotine technique is feasible, but, as with our clinical observations, the technique is associated with higher rates of haemorrhage.

When using the guillotine technique there was renal fracture 54% of the time under standard probe freeze–thaw cycles; 92% of the fractures were along the guillotine line. Increased ice-ball fracture and bleeding with the guillotine technique is consistent with our clinical experience, in which this technique results in a greater incidence of renal parenchymal fracture.

While it is important to know that the guillotine technique has a greater risk of bleeding, the technique remains useful for treating very cephalad upper-pole renal cortical neoplasms, $\approx 5\%$ of tumours in our clinical experience. Typically, we have been able to control bleeding during guillotine cryoablation procedures with gentle pressure and application of Floseal. However, the surgeon should be aware that bleeding is more common with the guillotine technique, and hilar exposure for temporary clamping if bleeding should be difficult to control might be indicated in some cases.

In conclusion, renal fracture and haemorrhage is a rare complication of renal cryoablation. Using smaller probes will help to minimize renal fracture, particularly when asynchronous probes are deployed. Large cryoprobes should be avoided, as they are the most likely to result in a renal fracture. Although the guillotine technique might be useful for upper pole renal ablation, it is associated with a greater risk of renal parenchymal fracture and haemorrhage.

CONFLICT OF INTEREST

Jaime Landman received Research support and is a Consultant.

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