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TECHNICAL NOTE

Microwave Ablation of Adrenal Tumors in Patients With Continuous Intra-Arterial Blood Pressure Monitoring Without Prior Alpha-Adrenergic Blockade: Safety and Efficacy

John F. Swietlik[1] · Emily A. Knott[1] · Katherine C. Longo[1] · E. Jason Abel[2] · Shane A. Wells[1] · Meghan G. Lubner[1] · Paul F. Laeseke[1] · Timothy McCormick[3] · J. Louis Hinshaw[1] · Fred T. Lee Jr.[1,4] · Timothy J. Ziemlewicz[1]

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Abstract

Purpose Evaluate the safety and efficacy of adrenal microwave ablation performed with continuous intra-arterial blood pressure monitoring (IABPM) and without alpha-adrenergic blockade (AAB) as pretreatment.

Material and Methods A single-center, retrospective review of all percutaneous adrenal microwave ablation performed between 2011 and 2018. Microwave ablation was completed on 11 patients, with a total of 15 adrenal tumors with a mean size of 3.3 cm (1.4–6.9 cm) treated metastatic RCC, HCC, esophageal carcinoma, adrenal adenoma. Cases were performed without prior AAB, but with continuous IABPM and rapid intervention using short-acting antihypertensive medications.

Results There were no post-procedural episodes of hypertension, no neurological or cardiovascular complications, and no SIR moderate or worse adverse event complications. Mean intraprocedural maximum systolic blood pressure (SBP) was 211 mmHg (range: 132–288), with an average increase in SBP of 100 mmHg (range: 23–180). A hypertensive crisis (SBP $\geq$ 180 and/or DBP $\geq$ 120) occurred in 9 of the 15 procedures (60%) with a mean length of 3.0 min (range: 1–12). The technical success rate was 100% (15/15 procedures). The mean follow-up time was 2.4 years (range: 0.9–7.7 years), with primary and secondary efficacy rates of 77% and 87%, respectively, and an overall survival of 82%.

Conclusion In this single-center retrospective study, microwave ablation of adrenal tumors without AAB was safe and effective when performed with continuous arterial line monitoring of vital signs and the use of short-acting, rapid-onset antihypertensive medications.

Level of Evidence Level 4, Case Series.

Keywords Ablation · Adrenal ablation · Interventional oncology

Introduction

Percutaneous ablation has been shown to be safe and effective for treating adrenal tumors [1–4]. However, most adrenal MW ablation literature has reported using alpha-adrenergic blockade (AAB) pretreatment, without continuous intra-arterial blood pressure monitoring (IABPM) or details regarding the physiologic response to adrenal heating by MW [5–9]. Adrenal heating and thawing can cause acute blood pressure (BP) elevations and tachycardia, which can be pretreated by AAB [10, 11]. AAB drugs are long-acting and associated with hypotension and reflex tachycardia which is problematic in patients with pre-existing cardiovascular disease [12, 13]. Additionally, AAB may blunt but does not eliminate the hypertensive response

✉ John F. Swietlik
jswietlik@uwhealth.org

[1] Department of Radiology, University of Wisconsin, 600 Highland Ave, Madison, WI 53792, USA

[2] Department of Urology, University of Wisconsin, 1685 Highland Ave, Madison, WI 53705, USA

[3] Department of Anesthesiology, University of Wisconsin, 600 Highland Ave, Madison, WI 53792, USA

[4] Department of Biomedical Engineering, University of Wisconsin, 1550 Engineering Dr, Madison, WI 53706, USA

[2, 9, 12, 14, 15]. In 2011, a multidisciplinary team created an adrenal MW protocol including real-time IABPM with rapid treatment of hypertension and tachycardia with short-acting antihypertensive medications. This study was completed to evaluate the safety and efficacy of percutaneous adrenal MW ablation performed under continuous IABPM without AAB.

Methods:

Patient Population

All adrenal MW patients from 2011 to 2018 were identified and reviewed under a waiver of informed consent from the IRB, identifying 11 consecutive patients (Table 1). Adrenal MW ablations were performed without AAB, but with continuous IABPM and short-acting antihypertensive mediations. 15 MW ablation procedures were completed on 11 patients. Procedures were defined as treatment of a single/multiple lesions during one session. 15 tumors were treated, with two patients requiring a second procedure and a single patient requiring 3 procedures for tumor control (Table 2). Tumor type and size were recorded (Table 1).

Outcome Definitions

Outcome definitions were based on published guidelines [16]. Primary technique success was defined as percentage of tumors without evidence of local tumor progression (LTP) throughout follow-up. Secondary technique efficacy was defined as tumors without evidence of LTP, or if LTP occurred, no further progression after repeat ablation. Follow-up time was time from initial ablation through most recent imaging or patient death. Tumor size and ablation zone size were given as longest 3-plane dimension.

Table 1 Patient demographics

Patient demographics	
Total patients	11
Patient sex (M:F)	(9:2)
Mean patient Age (range)	65 (44–79)
Total tumors	15
Tumor type:	
HCC Met	5
RCC Met	8
Adrenal adenoma	1
Esophageal Met	1
Total MW procedures	15
Mean largest Dimension tumor size (cm)	3.3 (1.4–6.9)

MW Ablation Technique

Ablations were performed under general anesthesia with continuous IABPM via arterial line. All procedures used a single MW ablation system (Certus 140; Ethicon, Inc. Madison, Wisconsin). Antenna placement was completed using CT fluoroscopy guidance (Optima CT 660; GE Healthcare, Waukesha Wisconsin), with non-contrast CT performed to confirm needle positioning prior to ablation (Figs. 1–2). Ablations were performed by radiologists with 5–20 years ablation experience. Treatment settings were at the discretion of treating physicians (Table 2). Ablations were stopped at first evidence of significant hypertension and short-acting antihypertensive medications were administered. Antihypertensive medications were given in bolus and continuous drip form, with type, delivery method, and dosage at the anesthesiologist's discretion. This cycle was repeated until the entire tumor was ablated. Post-ablation contrast-enhanced CT was obtained to evaluate tumor coverage and complications.

Electronic Medical Record (EMR) and Imaging Review

Data collected from EMR (Epic, Verona, Wisconsin) review included ablation settings, procedural notes, IABPM and ECG recordings, and peri-procedural medications. Post-ablation contrast-enhanced CT images were evaluated for technical success, ablation zone measurement, and complications. Imaging was obtained at 3, 6, 9, and 12 months post-procedure, then as needed per oncology. Images were reviewed in consensus with a radiology trainee and attending radiologist with 10 years' experience.

Blood Pressure Evaluation

BP elevations were defined as $>$ 20 increase in systolic blood pressure (SBP) or diastolic blood pressure (DBP) from patient's baseline. Number and length of BP elevations were recorded. Additionally, episodes of hypertensive crisis (SBP $\geq$ 180 and/or DBP $\geq$ 120) and length of time of hypertensive crisis were recorded. Any neurologic or cardiovascular symptoms, or significant ECG changes (ST-elevation or new onset of arrythmia) were recorded. Society of Interventional Radiology (SIR) adverse events classification system was used to grade procedural-related complications [17].

Table 2 Procedural results

Patient	Procedure #	Procedure date (dd/mm/yy)	Sex	Age	Tumor type	# of tumors treated	Largest tumor dimension (cm)	Ablation time (min)	# of cycles
A	1	9/14/11	M	65	L Met RCC	1	3.1	5	2
A	2	9/28/11	M	65	R Met RCC	1	4.3	5	5
A	3	8/15/12	M	66	Recurrence of R Met RCC & 2 new met RCC	3	2.0; 1.6; 1.8	15	3
A	4	5/24/17	M	71	Recurrence of original R Met RCC	1	4.1	5	2
B	5	6/20/12	M	79	Met HCC	1	6	12	6
C	6	11/18/15	M	70	Met HCC	1	3.3	10	3
D	7	1/13/16	M	44	Met RCC	1	4.3	6	1
E	8	7/20/16	M	65	Met RCC	1	1.5	6	2
E	9	2/8/17	M	66	Reccurrence of Met RCC	1	1.8	5	2
F	10	10/19/16	F	60	Met RCC	1	1.9	11.5	3
G	11	11/23/16	M	69	Met HCC	1	1.4	5	3
H	12	12/21/16	M	59	Met HCC	2	2.6; 3.8	13	10
I	13	9/20/17	F	56	Adrenal Adenoma	1	6.9	10	7
J	14	7/11/18	M	71	Met esophageal SCC	1	3.9	10	3
K	15	11/14/18	M	69	Met RCC	1	5.1	17	3

Patient	Baseline BP (mmHg)	Max BP (mmHg)	# HTN crisis periods	Avg time in HTN crisis (min)	Medications	Complications	Technical Success	FU time (years)	LTP	OS
A	109/71	132/90	0	NA	None	Small PTX	Y	7.7	None	Alive
A	122/76	217/117	4	5 min (range 1–12)	Nitroglycerin, Esmolol, and Labetalol	None	Y	7.7	Positive	Alive
A	123/80	168/91	0	NA	Labetalol	None	Y	7.7	Positive (recurrence of originally treated R Met RCC, 2 new Met RCC had no LTP)	Alive
A	110/67	147/84	0	NA	None	None	Y	7.7	None	Alive
B	113/53	288/136	3	3 min (range 1–7)	Nitroglycerin, Nitroprusside, and Labetalol	None	Y	1	None	Alive
C	113/66	265/102	1	5 min	Nitroglycerin and Labetalol	None	Y	2.9	Positive	Alive
D	111/65	167/90	0	NA	Nitroprusside and Esmolol	None	Y	3.4	Positive	Alive
E	119/63	262/94	1	2 min	Nitroglycerin	None	Y	1.9	Positive	Deceased (brain mets, stopped dialysis)
E	92/56	228/106	1	2 min	Nitroglycerin, Nitroprusside, and Esmolol	None	Y	1.9	None	Deceased (brain mets, stopped dialysis)
F	114/69	178/95	0	NA	Nitroglycerin and Esmolol	None	Y	2.6	None	Alive

Table 2 Procedural results

Patient	Baseline BP (mmHg)	Max BP (mmHg)	# HTN crisis periods	Avg time in HTN crisis (min)	Medications	Complications	Technical Success	FU time (years)	LTP	OS
G	102/64	267/93	2	2 min (range 1–3)	Nitroglycerin, Esmolol, and Labetalol	None	Y	2.6	None	Alive
H	106/64	286/133	3	3.3 min (range 2–5)	Nitroglycerin	None	Y	0.9	None	Deceased (liver HCC disease burden)
I	108/64	231/96	5	1.8 min (range 1–3)	Nitroglycerin and Labetalol	None	Y	1.2	None	Alive
J	105/66	192/82	1	3 min	Nicardipine and Esmolol	None	Y	1.0	None	Alive
K	107/60	133/80	0	NA	Nicardipine	None	Y	1.3	None	Alive

Met metastatic; *RCC* renal cell carcinoma; *HCC* hepatocellular carcinoma; *SCC* squamous cell carcinoma; *PTX* pneumothorax

Results

Ablation Results

Ablation results are summarized in Table 3. Three of four LTPs occurred at the anterior aspect of the right adrenal tumor along the posterior edge of the inferior vena cava (Fig. 2). Two of four patients with LTP did not undergo retreatment due to widespread metastatic disease on follow-up imaging, conferring a secondary efficacy rate of 87%. Overall survival was 82% (9/11 patients). Neither patient death was due to adrenal disease.

Physiologic Response (Table 4)

Mean baseline SBP before MW ablation was 110 mmHg (range: 92–123). Intraprocedural mean maximum SBP was 211 mmHg (range: 132–288), with average intraprocedural increase in SBP of 100 mmHg (range: 23–180). Mean number of episodes of SBP or DBP elevations > 20 per procedure was 3.9 (range: 2–10), with mean length of time per BP elevation of 5.0 min (range: 1–16). Hypertensive crisis occurred in 9/15 procedures (60%), with a mean of 2.3 (range: 1–5) hypertensive crisis episodes and mean length of time of hypertensive crisis of 3.0 min (range: 1–12) in those 9 procedures (Fig. 3).

Blood Pressure Medications (Table 5)

BP elevations were treated acutely with short-acting antihypertensive medications, including nitroglycerin (9/15 procedures), esmolol (6/15 procedures), labetalol (6/15 procedures), nitroprusside (3/15 procedures), and nicardipine (2/15 procedures). One procedure required no BP medication with intraprocedural maximum SBP of 132 mmHg.

Complications

There was no evidence of cardiac stress (significant ST-elevation or onset of new arrythmia) on intraprocedural ECG, or neurologic or cardiac symptoms. One patient experienced a small pneumothorax post-procedure not requiring any further intervention (SIR mild-adverse event) [17]. There were no moderate or worse complications per SIR adverse event classification [17].

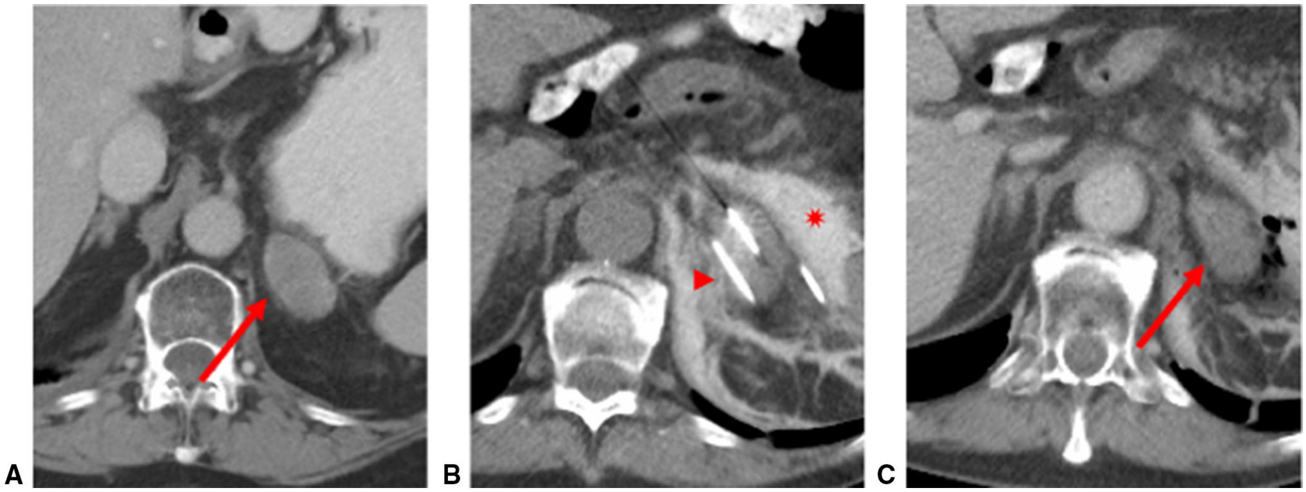

Fig. 1 Treatment of a 3.9 cm esophageal carcinoma metastasis in the left adrenal gland. Pre-ablation portal venous-phase image. **A**, the tumor (arrow) in close relationship with the stomach. Intraprocedural non-contrast image **B** shows antenna placement within the tumor (arrowhead) following hydrodissection (asterisk). Post-ablation portal venous-phase image **C** demonstrates successful ablation of the tumor without evidence of residual tumor (arrow).

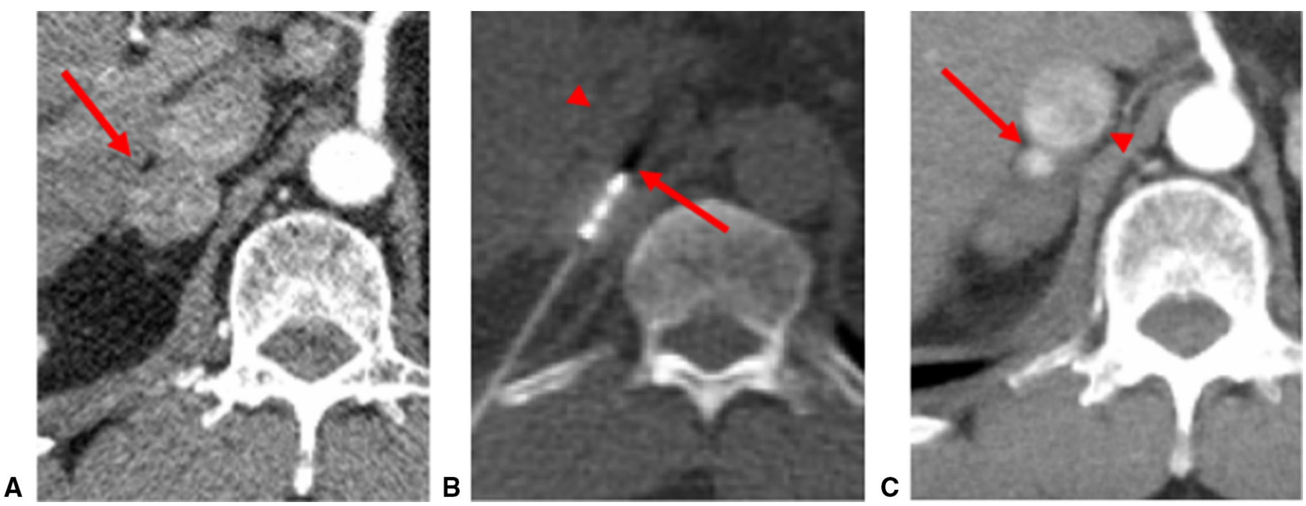

Fig. 2 Representative case of tumor recurrence. **A** Arterial phase CT image demonstrates a hyperenhancing 3.3 cm right adrenal hepatocellular carcinoma metastasis (arrow). **B** Intraprocedural non-contrast CT image showing the microwave antenna within the tumor but positioned short of deep border of the tumor adjacent to the IVC (arrowhead). Optimal positioning (arrow) would be with antenna tip just beyond the deep border of the tumor adjacent to the IVC to mitigate any heat-sink effect. **C** 6-month follow-up arterial phase CT image with recurrent nodule (arrow) immediately posterior to the IVC (arrowhead).

Discussion

In this retrospective study, MW ablation of adrenal tumors was performed with continuous IABPM, but without AAB. There were no cardiac or neurologic complications, no cases of post-procedural hypertension, and no cases of intra or post-procedure bleeding. Procedures had close cooperation between anesthesia and radiology with careful BP monitoring, immediate cessation of energy delivery with BP rise, and short-acting antihypertensive medications titrated to affect. After return to normotension, energy delivery was restarted until subsequent BP elevation. This cycle was repeated until the ablation was completed.

Mean maximum SBP and hypertensive crisis rate were higher than prior adrenal MW literature, but some patients received AAB and procedures were limited by the lack of IABPM [5–9]. BPs in this study were quickly corrected with a mean duration of hypertensive crisis of 3 min.

Differences in BP monitoring may explain the higher rates of hypertensive crisis as short elevations may go undetected if monitoring at 3–5 min intervals [2]. IABPM is more accurate and reliable than external measurements which can underestimate intra-arterial SBP, an effect which is amplified as SBP increases [18, 19]. Differences of > 20 mmHg can be seen with SBP above 160 mmHg [18, 19]. Hypertensive crisis rate in this study was comparable to large published cohorts of mixed modality adrenal ablations (43–46%), which occurred despite AAB for majority of patients [2, 15].

Surgical resection appears to provoke a larger physiologic response than MW ablation, which is only partially blunted with the use of AAB. 51–85% of surgical resections with AAB had hypertensive crisis, which was sustained for > 10 min in up to 25% patients [20, 21]. Despite the BP elevations, no perioperative deaths, myocardial infarctions, or cerebrovascular events were seen [20, 21].

Table 3 Ablation-specific parameters

Ablation-specific parameters	
Mean total active Ablation time (min)	9.0 (5–17)
Mean number of treatment cycles	3.4 (2–10)
Mean number of probes	1.8 (1–3)
Total number of procedures with hydrodissection	8
Technical success	15/15 (100%)
Mean follow-up time (years)	2.4 (0.9–7.7)
Local tumor progression	27% (4/15)
Primary efficacy rate	73% (11/15)
Secondary efficacy rate	87% (13/15)
Overall survival (n = 11 patients)	82% (9/11)

Importantly, BP elevations in the current study appear shorter than surgery, aligning with MW data and large mixed modality adrenal ablation cohorts [2, 5, 8, 9, 20, 21]. End-organ complications from BP elevations are related to some combination of degree of elevation and time. The short BP elevations in this study likely contributed to the lack of complications, but the exact relationship between these two variables is unknown.

The lack of control group limits the ability to compare adverse events to adrenal ablation completed after AAB. An additional limitation is the lack of standard intraprocedural hypertension treatment algorithm which varied at the discretion of anesthesiologist. Medications included short-acting nitrates, beta blockers, and calcium channel blockers or a combination, which evolved with experience over this study. Existing data on intraprocedural BP control during pheochromocytoma surgical literature suggest using a combination of nitroprusside, nitroglycerin, esmolol, and remifentanil [22]. Using short-acting beta blockers and nitrates for the treatment of hypertensive crisis is preferred to avoid hypotension once the catecholamine surge secondary to ablation subsides [23]. Optimization of a specific intraprocedural drug protocol is likely best studied in an animal model. Results from this study are from a single MW device and occurred with intermittent energy delivery, both of which could have an impact on outcome and is an area of future study.

Conclusion

In this single-center retrospective study, MW ablation of adrenal tumors without AAB was safe and effective when performed with continuous IABPM and rapid administration of short-acting antihypertensive medications.

Table 4 Intraprocedural blood pressure details

Intraprocedural blood pressure details	
Mean baseline systolic BP (mmHg)	110.3 (92–123)
Maximum systolic BP (mmHg)	211 (132–288)
Mean increase in systolic BP (mmHg)	100 (23–180)
Mean number of systolic or diastolic BP elevations > 20 per procedure	3.9 (2–10)
Length of time per BP elevation > 20 (min)	5.0 (1–16)
Percentage of procedures with hypertensive crisis (SBP ≥ 180 &/or DBP ≥ 120)	60% (9/15)
Mean length of time of hypertensive crisis episode (min)	3.0 (1–12)

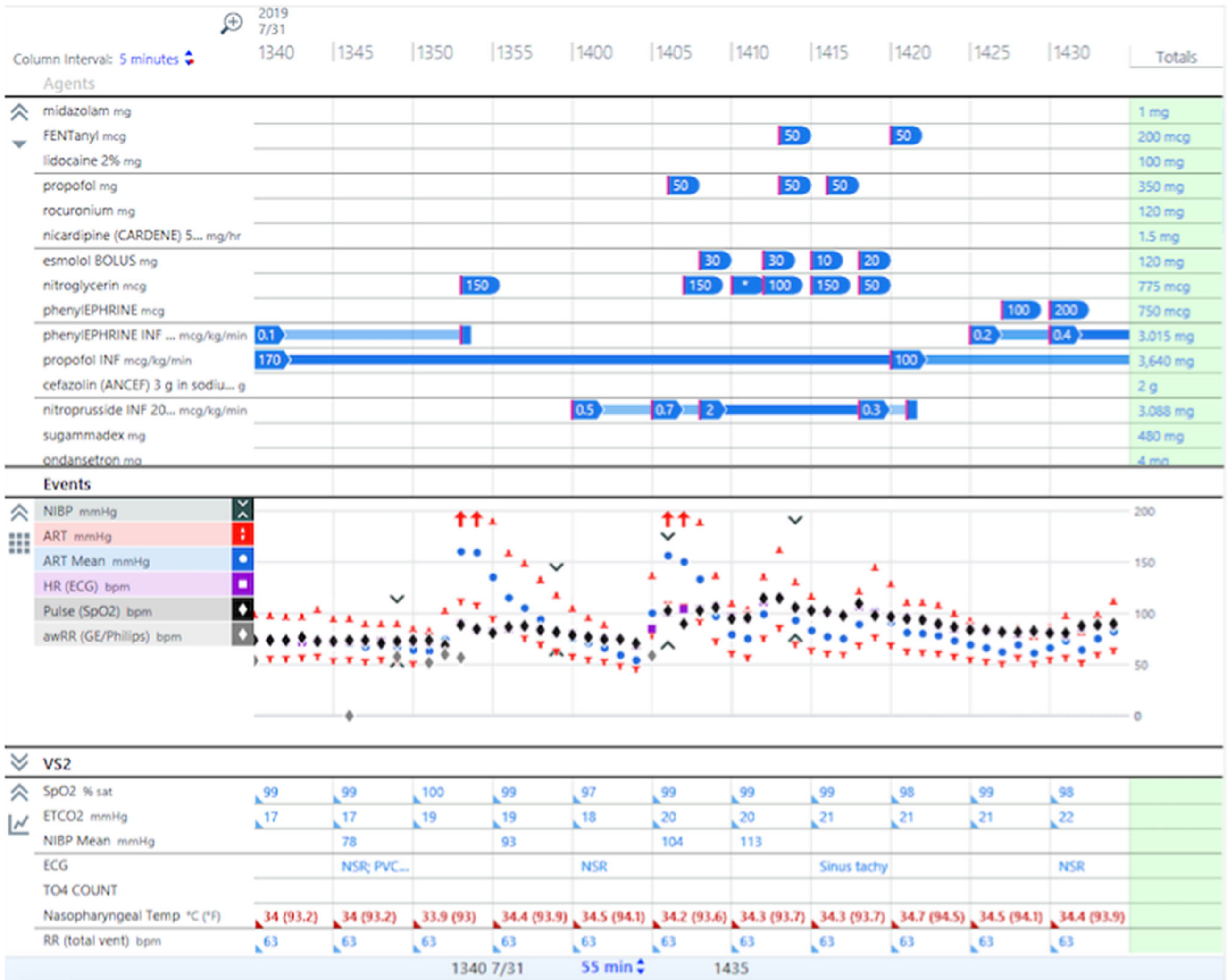

Fig. 3 Anesthesia flow chart demonstrates automatically recorded patient vital signs, including arterial pressures, and administered medications throughout an adrenal ablation. The flow chart showcases transient nature of the intraprocedural episodes of hypertension with the use of rapid-onset short-acting BP medications

Table 5 Intraprocedural medication details

Medications	Method of delivery	Mean total dose/procedure (range)	Total number of procedures drug used in (n = 15)
Nitroglycerin (mg)	Bolus	4.4 (0.1–22)	9
Nitroglycerin (mg)	Drip	4.6 (0.5–9.6)	4
Nitroprusside (mg)	Bolus and/or drip	4.9 (0.1–3.3)	2
Nicardipine (mg)	Bolus and/or drip	4.4 (3.2–5.5	2
Esmolol (mg)	Bolus	63 (30–120)	6
Labetalol (mg)	Bolus	17 (5–40) mg	6

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Compliance with Ethical Standards

Conflict of interest SAW receives consultant fees from Ethicon, Inc. MGL receives grant funding from Phillips and Ethicon, Inc. PFL receives consultant fees from Ethicon, Inc; The author receives consultant fees and is a stockholder in Elucent Medical; The author is a stockholder in Histosonics, Inc, McGinley Orthopedic Innovations; The author receives grant funding from Siemens Medical. JLH- The author receives consultant fees from Ethicon, Inc. The author is a stockholder in Histosonics, Inc, Elucent Medical, LiteRay, Accure,

and Cellectar. FTL Jr receives consultant fees from Ethicon, Inc. The author is a stockholder, is on board of directors, and receives research support from Histosonics, Inc. The author has patents with and receives royalties from Medtronic, Inc. The author is a stockholder and board observer in Elucent Medical. The author is a stockholder in Eximis Surgical. The author is a stockholder in Healthmyne, Inc. The author is a stockholder in ImageMover, Inc. The author is a stockholder in Zurex, Inc. TJZ receives consultant fees from Ethicon, Inc. The author is a stockholder in Histosonics, Inc. TM, JFS, EAK, KCL, and EJA declare that they have no conflicts of interest.

Ethical Approval For this type of study, formal consent is not required and was performed under a waiver of informed consent by the University of Wisconsin Institutional Review Board.

Informed Consent This study has obtained IRB approval from the University of Wisconsin Institutional Review Board and the need for informed consent was waived.

Consent of Publication For this type of study, consent for publication is not required.

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