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ORIGINAL RESEARCH **MONITORED ANESTHESIA CARE**

Monitored anesthesia care for percutaneous radiofrequency ablation of oncological lesions: a retrospective analysis and literature review

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ABSTRACT

Background & objective: Radiofrequency ablation (RFA) of solid tumors is a minimally invasive procedure intended to treat primary and/or metastatic, benign or malignant solid tumors; via thermal tissue destruction by means of targeted thermal energy guided coagulative necrosis. This procedure can be performed under sedation, general anesthesia (GA) or regional blocks. However, no defined modality exists. We analyzed the different anesthetic modalities and drug combinations which can provide optimal surgical conditions and a successful outcome. Secondary objectives were to analyze common adverse events associated with each anesthesia technique

Methodology: In this retrospective study, a total of 100 patients were included based on completeness of records, valid consent from 2008-2018. Outcome measures were; demographic characteristics, ASA status, comorbidities, anesthetic management including drug combinations used, pain management modality, and complications - both intra-operative and post-operative complications. Data was assessed and analyzed using descriptive statistics.

Results: Majority of the patients were male (55%), ASA physical class II/III (83%). Anesthesia drug combinations were classified as ketamine and non-ketamine based (85:15). Primary sites for RFA were liver (75%) followed by bone, kidney, adrenal and lungs. Main complications observed were pain and hypotension. Incidence of complications were higher in non-ketamine group.

Conclusions: Most cases of radiofrequency ablation can be performed successfully under sedation with local anesthesia. Despite being minimally invasive, it requires complete preparation with general anesthesia back-up, and pre-operative assessment/investigations. Ketamine based combinations exhibited better patient compliance with lower complication rates than non-ketamine-based combinations.

Abbreviations: GA - General anesthesia; MAC - Monitored anesthesia care; p-RFA - Percutaneous radiofrequency ablation; RFA - Radiofrequency ablation; TIVA - Total intravenous anesthesia;

Keywords: Keta-dex, Ketamine, Radiofrequency ablation, RFA, Pain, Sedation, Monitored anesthesia care, MAC

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1. INTRODUCTION

Cancer is a leading cause of death and poses a challenge to the healthcare systems world-over. There were an estimated 19.3 million new cancer cases and 10 million cancer-related deaths worldwide in 2020.[1] Managing this challenge, primary treatment modalities include either surgical or chemo/radiation therapy. However, since the year 2000 when the first case of Percutaneous Radiofrequency Ablation (p-RFA) of solid tumors was published, p-RFA has added another dimension in the treatment of solid tumors for whom surgical resection has always been considered as the gold standard.[2] However, surgical resection is not always an option, especially in patients with multiple co-morbidities or poor functional status where surgery could result in high morbidity and mortality.[3]

p-RFA of solid tumors is a minimally invasive procedure intended to treat primary and/or metastatic, benign or malignant solid tumors; via thermal tissue destruction by means of targeted thermal energy guided coagulative necrosis, thereby achieving tumor eradication.[4] Advantages of p-RFA include fewer complications, shorter hospital stay, and repeatability if recurrence occurs. However, the major problem associated with this procedure is the intra- and post-procedural pain while ensuring complete or minimal mobility so as to ensure accuracy in the procedure. As a result, team collaboration between interventional radiologist and anesthesiologist is prudent in planning and conduct of a successful p-RFA procedure.[5] Despite over 20 years of this therapy the anesthesiologists stay divided regarding choice of anesthetic modality to be employed. With no general consensus, perennial dilemma between the two most commonly used anesthesia modalities; General anesthesia (GA) or conscious sedation persists. Regional anesthesia (RA) techniques are gradually and deservingly demanding their share of pie.

The aim of this study was to retrospectively analyze and evaluate demographic factors, characteristics of lesions, anesthesia modalities used and the anesthesia drug combinations used along with associated complications, during or subsequent to an RFA procedure and possibly suggest the safer or better modality for patients undergoing p-RFA.

2. METHODOLOGY

2.1. Study design

This retrospective cohort study was conducted in a tertiary care oncological center. After approval from the Institutional Research Committee and Hospital Ethics Review Committee (RGCIRC/IRB/232/2018), all elective benign/malignant or metastatic lesions suitable for single or multiple setting p-RFA were considered from the year 2008 to 2018. This research was conducted in accordance with the Declaration of Helsinki and all efforts were made to ensure the anonymity of patients, whose records were analyzed. All patient records were reviewed and those with completed consent forms, pre-anesthesia check-up notes, preoperative, intraoperative and post-operative notes were included in the study and comprised the sample cohort. As for the review of literature, a comprehensive PubMed, MEDLINE and Google Scholar based search was made with key words 'Radiofrequency ablation'/'RFA', 'Anesthesia for RFA in cancer patients', 'microwave ablation'. and manuscripts published till date were considered. Case reports, case series and prospective/ retrospective studies were included in which any form of anesthesia modality for perioperative management of RFA was used.

2.2. Inclusion/ exclusion criteria

Cases were included on the basis of valid consent and completeness of records irrespective of the mode of anesthesia or drugs employed or the critical condition of the patient. Exclusion criteria included procedure being abandoned due to non-anesthetic causes or open RFA procedures.

2.3. Variables evaluated

The data was recorded on a predesigned form approved by the ethical committee with respect to the patient demographic data, associated comorbidities, site/duration or cycles of p-RFA, anesthetic technique employed, any intra-operative difficulties or complications and post-procedure outcome. Demographic characteristic, ASA physical status, comorbidities, anesthetic management, pain management modality used, and complications (intra-operative and post-operative) were documented. Bradycardia was defined as per the Advanced Cardiac Life Support criteria of less than 50,[5] while hypo/hypertension was defined as ± 30% variability from the baseline.[6] Pain was defined as all patients with Visual Analogue Scale score more than equal to 4.[7]

2.4. Statistical analysis

Frequency and percentage were computed for qualitative observation and were analyzed by Chi-square test. Mean ± standard deviation and median (interquartile range) were presented for quantitative variables and were analyzed by independent sample *t*-test.

3. RESULTS

Anesthesia records of 100 patients who underwent RFA were analyzed. Demographic profile was analyzed and has been reflected in Table 1. Patients undergoing p-RFA exhibited male predominance (55%) with the mean

Table 1: Demographic profile of the patients

Parameter	Result (n = 100)
Age (y)	51.33 ± 18.24
Body Mass Index (kg/m^2)	24.37 ± 5.75
Sex (Male: Female)	55:45
ASA Class	
• I	09 (9)
• II	39 (39)
• III	44 (44)
• IV	08 (8)
Chemotherapy/radiotherapy Status	
• Post Chemotherapy	37 (37)
• Post Radiotherapy	20 (20)
Child Pugh Status	
• Child Pugh A	80 (80)
• Child Pugh B	20 (20)

Data presented as mean ± SD or n (%)

Table 2: Lesions/RFA characteristics

Lesions	Complications [n (%)]
Location of RFA	
Liver	75 (39)
Bone (Pelvis/Radius/Femur/Tibia/ Coracoid)	19 (01)
Adrenal	01 (01)
Kidney	02 (01)
Lung	03 (01)
Number of Lesions	
1	94 (41)
2	06 (02)
>2	00 (00)

age being 51.33 ± 18.24 years having a Body mass index of 24.37 ± 5.75. Patient distribution as per ASA physical status undergoing RFA were ASA I/II/III/IV: 9/39/44/8 (Table 1).

Predominant site of p-RFA was liver lesions (either primary hepatocellular carcinoma or metastasis from other primary sites of malignancy) with 75 percent patients followed by bone lesion ablations; osteoid osteoma (15%) and bone metastatic lesions (4%). Remaining sites of p-RFA were kidney (2%), lung (3%) and adrenal (1%) (Table 2).

Approximately a third of patients (37%) had undergone chemotherapy and 1/5th (20%) had undergone radiation therapy for the primary pathology. Eighty percent patients belonged to Child Pugh A class and remainder

Table 3: RFA and anesthesia features

Parameter	Result
Duration (min)	
RFA	37.42 ±15.91
Anesthesia	50.06 ± 16.33
Type of Anesthesia administered	
Sedation	95 (95)
Sub Arachnoid Block	05 (05)
Positioning	
Supine	87 (87)
Lateral	05 (05)
Prone	06 (06)
Semi-prone	02 (02)

Data presented as mean ± SD or n (%)

were of Child Pugh B category. Ninety-four patients had single lesion p-RFA while the rest had more one lesions undergoing p-RFA (Table 1).

Mean duration of radiofrequency ablation was 37.42 ± 15.91 min while mean anesthesia duration was 50.06 ± 16.33 min. Majority of patients (95%) underwent p-RFA under monitored anesthesia care (MAC) with total intravenous anesthesia (TIVA) while for 5 patients subarachnoid block was employed. None of the patients required complete endotracheal or laryngeal mask airway GA (Table 3).

As many as 8 combinations were employed by different anesthesiologists for conducting a successful p-RFA. Number of patients exposed to each combination along with the complications associated with each combination have been highlighted in Table 4.

Eighty five percent of patients were administered ketamine-based combinations while rest were administered non-ketamine-based anesthesia. Most common postoperative complication encountered was pain at the RFA site (21%). Of 21 patients 13 patients were administered a non-ketamine-based combination, e.g., propofol/fentanyl or propofol/fentanyl/dexmedetomidine combination while remaining were administered ketamine-based combinations. One patient developed respiratory arrest subsequent to pneumothorax. Post procedural sedation was common in patients who had longer RFA/anesthesia durations, or ≥ 2 lesions or were administered a 4-drug combination (propofol/ketamine/fentanyl/dexmedetomidine) (Table 4).

4. DISCUSSION

p-RFA is a minimally invasive technique based on thermal destruction of tissue by administering

Table 4: Anesthesia drug combinations and complications

Drug combination		Hypo-tension	Hyper-tension	Sedation	Pain	Bradycardia	Respiratory arrest	Other (surgical)
Non-ketamine group	PF (12)	01			10			
	PFD (03)	03			03	01		
Ketamine group	PKF (21)		01		01			
	KFD (10)	01			01			01
	PKFD (24)			09	01		01	02
	K (06)				02			
	KF (08)			01	01			
	KD (16)			01	02			

Ketamine Group: PKF-propofol/ketamine/fentanyl; KFD-Ketamine/fentanyl/dexmedetomidine; PKFD-Propofol/ketamine/Fentanyl/dexmedetomidine; K-ketamine alone; KD-Ketamine/dexmedetomidine; KF-Ketamine/fentanyl. Non-Ketamine Group: PF: propofol/fentanyl; PFD: Propofol/Fentanyl/Dexmedetomidine)

electromagnetic energy. The procedure has good outcome, low mortality and high efficacy, with many patients being treated as per day care protocols with efficacious utilization of healthcare resources. Providing a calm, pain-free, immobile patient capable enough to obey commands are the major challenges faced by an anesthesiologist.

Even though p-RFA is performed across the world mainly under sedation or GA, regional anesthesia and truncal blocks are gaining popularity owing to better peri-procedural pain management with fewer opioid related side effects. However, there are no established protocols and drug combinations for the conduct of these procedures, different anesthesiologists employ different drug combinations and techniques involving sedative-hypnotic drugs along with opioid/non-opioid analgesics; proper administration/titration and balancing/scaling-up of sedation/analgesia with the level of stimulus administered remains a challenge. Commonly used anesthetic drugs include propofol, fentanyl, ketamine and dexmedetomidine along with midazolam, glycopyrrolate with/without fentanyl patch in varying combinations. The main focus of this retrospective analysis was to evaluate and analyze different combinations of anesthetic sedative-hypnotics and analgesic medications and find the safest and most efficacious of all combinations used.

A total of 8 drug combinations were employed; 2 combinations were non-ketamine based and 6 were ketamine-based combinations. Most common complication observed was pain in the peri-operative period in 21% of the patients. Next most common side effect was post-procedural sedation observed in 11/100 patients. While none of these patients were from the non-ketamine group, 9/11 patients were from the PKFD group and 1 each from KF and KD group. This can probably be due to the additive sedative effect secondary to concurrent/sequential administration of 4 sedative/hypnotic/analgesic drugs. In terms of side effect incidence, of the 15 patients of non-ketamine group; 13 developed anesthesia related side effects, the corresponding number in the ketamine group was much lower (18/85), and if the number of patients exposed to the 4-drug regime are removed, the number reduces further. This indicates the safety and efficacy of ketamine-based regime over the propofol/fentanyl-based regimes.

Apart from intra-operative concerns a meticulous pre-operative evaluation and post-operative pain management are the cornerstones of perioperative care in patients undergoing RFA, as these patients often have compromised physical status owing to the comorbidities and post-chemotherapy/radiotherapy status.[8] These patients should undergo a complete pre-operative evaluation and should be investigated as per established ASA standards and protocols; which includes hematological and biochemical investigations along with ECG and chest X-ray and if warranted special investigations such as echocardiography or pulmonary function tests.[8] Intra-operative monitoring standards should be as per protocols laid down by the ASA and should include ECG, pulse oximetry, end-tidal CO_2 and non-invasive blood pressure (invasive blood pressure if indicated). Our institute adhered to the ASA/Indian Society of Anesthesiologists (ISA) protocols in terms of pre-operative testing, fasting and intra-operative monitoring in all patients.

Shamim et al. retrospectively analyzed 46 patients who underwent p-RFA for hepatocellular carcinomas. They had conducted 40/46 cases under GA with a supraglottic device and remaining under sedation. While the predominant sex was female in their study, the predominant patients were of ASA II/III patients belonging to Child-Pugh class A which was similar to

our findings. Shamim et al. used propofol-fentanyl combination and majority of their patients experienced pain as the most common side effect which is similar for patients in our study who had received same regime.[8] In contrast the patients in our study who received ketamine-based regimes experienced lesser pain. In another retrospective analysis conducted by Amornyotin et al. in 400 patients, the demographic profile was similar to our patients.[9] They conducted majority (397/400) cases under sedation similar to ours successfully. While there was no comment on the combinations used, the predominant drugs employed were midazolam, fentanyl and propofol for successful conduct of p-RFA. No comment was made on the peri-operative pain management or pain as most common problem encountered, but they highlighted hemodynamic side effects as the most frequent side effects. In our case pain was the predominant perioperative problem; hemodynamic complications like hypotension/bradycardia were mainly encountered in the non-ketamine group as by Amornyotin et al.[9] Kim et al. evaluated GA vs sedation (n = 41 vs n = 10) for p-RFA of renal cell carcinoma. They concluded GA to be a better anesthetic technique for this procedure, which was contrary to our findings. Their study was, however, limited by the fact that only 10 patients were exposed to sedation as compared to 41 in the GA group.[10]

Elyazed et al. attempted p-RFA of hepatic lesions under right paravertebral block. However, they still needed sedation as the truncal block could not provide complete pain relief of shoulder pain due to ipsilateral parasympathetic innervation and contralateral sympathetic innervation. Thereby proving regional anesthetic techniques are not completely effective as compared to GA/sedation.[11] Mostafa et al. evaluated erector spinae plane block (ESPB) with sedation for hepatic RFA and conclusions were similar to Elyazed.[12] Gazzera evaluated role of paravertebral block during percutaneous transhepatic thermoablation, and despite complete technical success, 33% of the patients reported inadequate pain relief; which was similar to other studies in which thoracic paravertebral block (TPVB) was given.[13] Regional anesthetic techniques can't be used as sole anesthetic technique, but require sedation for better management of pain. However, they do provide better post-operative pain relief. In contrast to all other studies evaluating TPVB, Kim et al. concluded TPVB may be an effective and safe anesthetic method for decreasing or eliminating pain during and after RFA for hepatic lesions and helpful in decreasing the opioids use.[14] The findings were similar to that of a preliminary case series conducted by Piccioni et al. on 12 patients who underwent p-RFA of hepatic lesions under TPVB.[15] Choi et al. evaluated the effects of TEA during p-RFA for hepatocellular carcinoma. They concluded that TEA was associated with shorter procedure times, lower postprocedural pain, and lower opioid consumption during and after p-RFA, thus establishing efficacy of TEA on not only sedation techniques but also making it regional anesthesia technique of choice over TPVB, and a competitor for GA/sedation.[16] Ghallab et al. compared TIVA + face mask with inhalational anesthesia administered through supraglottic airway device, and compared intra-procedural hemodynamics and time for recovery/discharge. They concluded better hemodynamic control in patients with TIVA without complications like pain, vomiting, apnea, or prolonged ICU stay and discharge.[17] Amornyotin et al. in a prospective study compared propofol based deep sedation with or without midazolam for RFA in patients with hepatocellular cancer and concluded that there was no role of midazolam in anesthesia outcomes following RFA.[18] Wu et al. evaluated in a prospective study evaluated different effects of oxycodone and remifentanil in patients undergoing ultrasound-guided p-RFA of hepatic cancer and concluded oxycodone provided better patient experience with higher satisfactory score and less unwanted body movements, relieved post-procedural pain better, and not associated with an increase in adverse effects.[19] Yokoyama et al. evaluated conduct of RFA in cases of hepatocellular carcinoma through a prospective study with pain control obtained either by one-shot delivery and the continuous infusion of fentanyl in patients, and concluded that the later was better for pain control in patients undergoing RFA in the perioperative period.[20]

Piccioni et al. outlined minimum mandatory equipment requirement for p-RFA. For airway management; oxygen source with flowmeters, nasal cannula/mask with capnography, nasopharyngeal and oropharyngeal airways, supraglottic airway devices, bougies and stylets, self-inflating bag, endotracheal tubes and laryngoscopes with blades. All emergency medications with resuscitation drugs and drugs for GA along with specific reversal agents and local anesthetics should be available. [4] Monitoring standards as laid down by national/international anesthesia regulatory bodies should be adhered to and should include ECG, non-invasive blood pressure/ invasive blood pressure compatible monitors, capnography, temperature probes and pulse oximetry is mandatory. Suction apparatus and defibrillator for managing with emergencies should be available. Piccioni et al. also outlined the preferred positioning, anesthesia concerns and most frequent anesthesia complications in his research.[4] All cases of p-RFA regardless of site of lesion can be conducted under GA, sedation/local anesthesia + monitored anesthesia care (LA-MAC) as was seen in our analysis and that by Amornyotin et al.[9] p-RFA of hepatic lesions which are by far the most common and hence most studied can also

be performed under GA or thoracic paravertebral/epidural block (TPVB/TEA) and ESPB with sedation, while the main anesthesia concerns are pain, and need for breath holding.[4,9,11-16] In cases of p-RFA of kidney/adrenal, while the main concerns are difficult airway management in prone position; patients undergoing p-RFA of adrenal gland may occasionally experience hypertensive episodes, which was also observed in the sole case of adrenal gland RFA in our study.[4,10] Regional techniques have not been advocated in renal/supra-renal RFA.[4] In p-RFA lung regional anesthesia techniques TPVB/TEA and intercostal nerve blocks may be employed.[4] In p-RFA of bone lesions even though the literature does not support regional anesthesia, our research indicates successful conduct of tumor ablation under sub-arachnoid block.

5. LIMITATIONS

While our retrospective study included 100 subjects conducted in a premier oncology institute, no study is without limitations and so is the case with ours. First, the analysis was retrospective in nature and thus inferior to the data offered by the prospective studies. A need for protocol based prospective study in this field is the need of the hour for better generalization of data and guideline formulation. Also, retrospective data may result into underreporting of the adverse events. In view of multiple anesthesiologists following multiple protocols a standardization is not possible, as comfort / familiarity of each anesthesiologist with different drugs varies, which may also contribute to under reporting of adverse events.

6. CONCLUSION

p-RFA is a minimally invasive technique with good efficacy, compliance and results. However, the procedure requires a compliant, pain-free patient and requires harmonious coordination between the radiologist, anesthesiologist and the patient. Even though multiple anesthesia modalities including general anesthesia, regional anesthesia and sedation have been tried, no consensus has been reached and a tussle continues not only between GA and sedation but also the drug combination for providing sedo-analgesia. As per our retrospective study, pRFA can be performed safely under sedation is an effective modality in most cases with only handful of side-effects and general anesthesia may not be pre-requisite; especially as all patients may not be fit for general anesthesia. Even though propofol based or non-ketamine-based sedation regimes have been advocated by multiple authors, we conclude that ketamine-based regimes provided better surgical and anesthetic conditions and pain relief for the patient. Ketamine along-with dexmedetomidine (Keta-dex) should be evaluated for non-operating room anesthesia (NORA) for painful procedures like biopsies/RFA etc. as none of the two drugs causes respiratory depression or blunting of protective airway reflexes, both possess analgesic properties, and are devoid of opioid related side-effects and counterbalance each other's limitation/undesirable effects.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

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9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

AP: Concept, conduct of study work, manuscript editing

AM: Conduct of study work

VJ, VS: Manuscript editing

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