



Sedation and Analgesia Planning for HIFU Ablation

In this lecture, we are going to learn the current sedation and analgesia regimens for HIFU ablation of uterine fibroids and adenomyosis and the relevant precautions. The application of sedation and analgesia in HIFU ablation has greatly improved the clinical safety and reliability of HIFU procedure.

This lecture consists of four parts, 1. introduction of sedation and analgesia, 2. pre-operative preparation for sedation and analgesia, 3. intra-operative sedation and analgesia regimen, and 4. associated risks and complications of sedation and analgesia and corresponding prevention and risk management.

I. Sedation and analgesia for HIFU ablation

According to the American Society of Anesthesiologists, sedation and analgesia is intended to relieve the discomfort of patients, maintain the patients in good cardiovascular function without using ventilators to control their respiratory functions, and to keep the patients in conscious state so that they can communicate effectively with the doctor during a procedure.

The choice of anesthesia regimens are based on operation principles. Generally speaking, for conventional invasive and minimally invasive surgeries such as open surgery or laparoscopic surgery, general anesthesia or intraspinal anesthesia is used. Because such surgeries resect the target lesion by insertion of surgical instruments into patient's body, general anesthesia is required to block the sense of pain and maintain muscular relaxation in the surgical site.

While during the noninvasive HIFU ablation, it is critical to prevent the injuries of normal tissue and structures from the ultrasound energy deposit in the front and rear sound field, and therefore sedation and analgesia is needed to retain the patient's sensation and keep the patient in conscious state so that they can communicate effectively with the doctor during the procedure.



Sedation and analgesia is also used in surgeries such as painless tooth extraction or interventional embolization; or in the course of resection of small breast masses. For such operation, besides local injection of lidocaine, some sedative and analgesic agents are also given to make the patient more comfortable. However, these operations do not require strict control of sedation level. and it does not matter if the sedation level is a little deeper. As long as the patient can maintain adequate spontaneous ventilation without affecting their respiratory function and oxygen saturation, the sedation level can be deeper than that of HIFU

Nevertheless, the sedation level for HIFU ablation should be strictly controlled. On the one hand, shallower-than-intended level of sedation may make patients feel uneasy or pain during treatment and thus move their body on the treatment table. On the other hand, deeper-than-intended level of sedation may risk the safety of treatment. For example, as over-sedated patient cannot feel burning of skin, discomfort in the legs or loses sensation in the lower limb muscles, the patient will not communicate any discomfort to the doctor on the spot, which may result in blisters and ulceration on the skin, or even disruption of motor sensation as a result of nerve irritation.

The Guidelines for Procedural Sedation and Analgesia (PSA), published in the European Journal of Anesthesiology in 2018, specifies the requirements for the persons to implement sedation and analgesia. First, the specialists performing sedation and analgesia should be certified for and proficient in cardiopulmonary resuscitation (CPR). Second, the specialists should be able to perform pre-procedural clinical assessments, airway management and management of different levels of sedation, and have detailed knowledge of the pharmacology of drugs used for PSA and the monitoring devices and interpretation of the information provided by the monitors. Third, the specialists should have detailed knowledge of the major type of complications and their management.

Sedation and analgesia should be performed where an anesthetist is immediately available. In terms of dietary preparation, 2 hours before HIFU ablation, the patient can only take clear fluids such as water. Liquid diet such as milk, dairy food or drinks containing solid, grains or pulp should be avoided. 6 hours before HIFU ablation, the patient cannot take solid food. If sedation and analgesia is performed by HIFU doctors



instead of an anesthetist, they must have attended special training on sedation and analgesia authorized by professional organizations.

II. Pre-operative Preparation for Sedation and Analgesia

Pre-operative preparation for sedation and analgesia includes preparation of patients, drugs and devices.

Preparation of patients is intended to evaluate their pre-operative test results and to learn the medical history of underlying conditions such as hypertension, heart disease, or experience of anesthesia-induced complications. Inquiry of experience of anesthesia-induced complications is often overlooked or omitted by the doctors. We recommend that you may follow the following scheme to communicate with patients: 1. Have you had any surgery? 2. have you experienced any emergencies or been sent to intensive care unit for any special reason during and after a surgery? Have you been informed of any irregularity during the surgery?

Lab tests show that the levels of electrolytes are normal when they are admitted to the hospital for HIFU ablation. However, it should be stressed that more than 90% of patients may have significant loss of potassium after strict pre-operative bowel preparation, so throughout the perioperative period, it is important to supplement electrolyte for patients and observe the symptoms related to electrolyte deficiency, the liver and kidney function and the routine blood test results.

Furthermore, whether the patients have acute or chronic bleeding should also be confirmed. In case of acute bleeding, HIFU ablation is not recommended when the level of hemoglobin is low, unless the patient agrees to receive a blood transfusion before HIFU. In fact, the invasiveness of conventional open surgeries and minimally invasive surgeries which may require a blood transfusion is the reason why many patients with uterine fibroids or adenomyosis come for HIFU treatment. On the other hand, for patients with chronic bleeding, HIFU ablation can be conducted at a right time when the cardio-pulmonary function capacity of patients is sustainable.

Next, doctors need to assess the airway patency of patients. First, doctors should examine the patients' appearance and observe if there are any malformation, scars or



wounds. If the patient has undergone surgeries or got injured on her head or face, the scars or wounds may limit the openness of her mouth. And small mouth openness will pose some difficulty in conduction of cardiopulmonary resuscitation(CPR) or assisted ventilation.

In addition, assess the airway patency of patient using the 3-3-2 principle. 3 means that the mouth openness is not narrower than 3-finger width and that the distance from the jaw to the hyoid bone is not narrower than 3-finger width. 2 means that the distance from the hyoid bone to the cricoid cartilage is not narrower than 2-finger width. The 3-3-2 principle also applies to the situation where the patient suffers from respiratory depression and thus assisted ventilation or even tracheal intubation is required.

After the assessment of airway patency with the 3-3-2 principle, doctors need to examine the flexibility of patient's neck. Instruct the patient to lift her head up backward as much as possible. Some patients may have some neck problems or cervical disc herniation, which is likely to limit neck movement. Last but not the least, examine the size of tongue. Ask the patient to stick out her tongue and observe her hard palate, soft palate, uvulae etc. to see whether the tongue is too big. When the patient is asleep or in sedation, the tongue is likely to fall back like a cotton ball blocking the entire respiratory tract and spontaneous ventilation.

If the patient presents multiple problems mentioned above, she is likely to have respiratory depression and it may be difficult to conduct emergency treatment on her with current assisting approaches when she is in overdosed sedation. Therefore, special attention must be paid to the airway patency of patient. This slide summarizing airway patency assessment is deemed the second most important slide in this lecture and thus needs to be emphasized.

The assessment of special patients. The seven types of patients (A to F), listed below, can not be managed by HIFU doctors alone who have received training on sedation and analgesia for HIFU ablation. These patients must be inquired, evaluated, and managed jointly by HIFU doctors and anesthetists. As a HIFU doctor, you must know what you can do and what you cannot, do not take all the work on yourself.



Contraindications for sedation and analgesia include the following conditions: 1. patients allergic to sedative and analgesic agents; 2. patients with severe cardiac diseases; 3. patients with pulmonary dysfunction; 4. patients with renal insufficiency; 5. patients with severe liver failure; 6. patients suffering from cerebrovascular accidents in the recent three months; 7. patients unwilling to cooperate or with difficulty in communication and expression. These patients cannot receive sedation and analgesia and should therefore be reevaluated to determine whether they are suitable for HIFU ablation.

In addition to assessment of patients, pre-operative communication is also very important. It is aimed at informing patients of sedation and analgesia implementation in order to relieve their stress reaction and tension during operation. Meanwhile, doctors need to reassure patients and help them eliminate their concern over the normal or abnormal physical discomforts during operation, and encourage them to have an effective communication with the operator and cooperate with treatment.

Before treatment, doctors need to inform patients of the purpose of sedation and analgesia, the possible pain location, and the normal and abnormal intra-operative pain. Sedation and analgesia is intended to relieve the intra-operative pain and discomfort while preserving the sensation of abnormal discomfort. In addition, doctors should tell patients how to cooperate with treatment and coach them the methods of communication during operation. For example, the patient can use certain gestures and tools to communicate effectively with operators.

Operators should understand the characteristics of the pain during HIFU ablation, so that they can predict the time and degree of intra-operative pain and then determine the dosage of anesthetics correspondingly. In addition, operators should know the possible side effects associated with the dosage of sedatives and analgesics, such as respiratory depression and the degree of respiratory depression, etc. And they also need to know when nurses need to be in presence to administer anesthetics or to comfort the patient and help the patient stay in the best state for HIFU ablation.

The characteristics of pain associated with HIFU ablation. First, during HIFU ablation, patients with adenomyosis may feel more pain than patients with uterine fibroids. Generally speaking, most patients with uterine fibroids do not feel much pain



during treatment. However, some fibroid patients may feel obvious distending pain in the sacrococcygeal region because the sacrum and coccyx are exposed to more ultrasound energy in the rear sound field if uterine fibroid is close to them. For adenomyosis patients, our long-term clinical observation indicates that intra-operative pain is positively associated with the course of menstrual pain and the menstrual pain score (VAS score).

In addition, patients may feel pain immediately after HIFU ablation. Although treatment ends and no more ultrasound enters the patient's body, some heat still remains inside the body and the ultrasound energy has not been completely metabolized. So fibroid patients may feel a tolerable distending pain in the abdomen, like the distending pain before menstrual period. If the patient has experienced severe discomfort in sacrococcygeal region during HIFU, she would still feel obvious discomfort there after HIFU. Doctors need to pay special attention to such patients and observe whether they have any obvious delayed neuromuscular reaction in the lower limbs.

For adenomyosis patients, the post-treatment pain peaks in 4 to 6 hours after HIFU ablation, and the degree of pain resembles that of menstrual pain. For example, if the menstrual pain score of the patient is 8 points, and it is very likely that the post-treatment pain score can reach 8 points in the following 4 to 6 hours after HIFU. Therefore, doctors must pay attention to the post-treatment pain of adenomyosis patient in the following 4-6 hours after HIFU procedure and take some pain relief measures in advance or according to post-treatment observation, otherwise the patient may feel obviously uncomfortable.

Preparation of drugs include sedative and analgesic agents and their antagonists, as well as auxiliary drugs. Fentanyl and midazolam are most commonly used sedative agent and analgesic agents for HIFU ablation. The antagonist to fentanyl is Naloxone, while the antagonist to midazolam is Flumazenil. Auxiliary drugs include anti-allergic agents and some routine first-aid drugs. These drugs are all indispensable for HIFU procedure.

After a single injection of fentanyl, it takes about 5 to 6 minutes to reach its peak effect, with the effect lasting 25 to 30 minutes, while midazolam also takes about 5 minutes to be effective, lasting about 30 minutes. Please note that administration of fentanyl and midazolam at the same time will result in superposition of peak side effects in 5 minutes; both drugs can cause respiratory depression. Therefore, fentanyl is



administered before administration of midazolam in clinical practice to avoid the superposition of peak side effects.

Preparation of devices. In a HIFU procedure room, ECG monitor and oxygen supply are all necessary. It should be emphasized that for treatment of non-malignancies or benign tumors, manual ventilator and oropharyngeal airways must be equipped in the HIFU procedure room instead of somewhere in the preparation room or other department, as these devices may be used at any time.

In particular cases, it is advised to prepare laryngoscope, laryngeal mask and defibrillator. If possible, all the above mentioned devices can be prepared in the HIFU procedure room.

III. Implementation of sedation and analgesia during HIFU procedure

Evaluation of sedation depth summarized in this slide is one of the most important ones in this lecture. Our clinical observations indicate that sedation is more associated with the complications of HIFU treatment than analgesia. Deeper-than-intended level of sedation may restrain the patient from reporting skin burn or the neurological discomfort in lower limbs because she cannot feel it. Therefore, it is important for doctors to be proficient at evaluation of sedation depth which affords flexible use of drugs to reach the desirable sedation depth.

A newly set-up HIFU Center is recommended to follow a standard flowchart of administration of sedative and analgesic agents, ensuring the safety and simplicity of administration. With the experience of completing hundreds of cases when doctors can understand better the expected status of patient during HIFU ablation, sedatives and analgesics can be optimized to provide more comfort during treatment without raising the safety risk.

Evaluation of sedation depth. The sedation depth can help to determine administration of drugs and assess the safety of patient during HIFU treatment. Ramsay Sedation Scale with numerical score from 1 point to 6 points is used. The bigger the number is, the deeper the sedation is. During HIFU ablation, sedation level of 3 or 4 is



sufficient and recommended for ensuring both the safety of treatment and the comfortableness of patient.

When the patient is in sedation of level 1 or 2, her eyes are open; in sedation of level 3, her eyes are closed but will open briskly to gentle verbal command; in sedation of level 4 the patient does not respond to gentle voice but will open her eyes to shout or pat on her shoulders and can engage in verbal communication. If the patient does not respond, she may be in sedation of level 5. When the patient is asleep, she is in sedation of level 6 or deeper where HIFU ablation is not recommended.

This is the flowchart of administration of fentanyl and midazolam. 30 minutes after the first dose follows the second dose, and then 30 minutes after the second dose follows the third dose, and then the fourth dose will be given after 40 minutes.

This is a classic regimen and is recommended to the newly set-up HIFU Centers. Its advantages include being easy to operate by non-anesthetists and safe. Dosage of drugs can be easily calculated according to the weight (Kilogram) of the patient. By now, no respiratory problems associated with implementation of this sedation and analgesia regimen have been observed if this protocol was strictly followed. However, it also has some disadvantages. First, sedation effect of midazolam varies among different patients, which is a characteristic of midazolam. Patients of the same age and weight may reach different sedation levels after administration of the same dose of midazolam. For example, one patient may be in sedation of level 1, while another may be found at level 4. Second, there may be strong respiratory movement causing obvious abdominal displacement, which influences the precision of locating the target and consequently reduces treatment efficiency. Third, the effect of this regimen is unsatisfactory on the adenomyosis patients with high menstrual pain score or the patients with uterine fibroids close to the sacrum.

Here are some other regimens for your consideration, in which the drugs can only be administered by anesthetists. Anesthetists and operators should remember not to use Propofol as sedatives, because its sedation effect is completely uncontrollable.

This is a well-developed regimen of Dexmedetomidine and remifentanyl, used in Chongqing Haifu Hospital, which should be implemented only by anesthetists. As remifentanyl has short potency, insufficient post-treatment pain relief will make the



patient feel much discomfort in the following 4 to 6 hours after HIFU ablation. Therefore, when using this regimen, anesthetists must complete both intra-operative and post-operative analgesia.

The advantages of this regimen include easy administration of drugs, stable sedation depth at Ramsay Score of 3 or 4, less impact on breathing and good analgesic effect. Its disadvantages are: 1. it can only be implemented by anesthetists, 2. remifentanil should be given immediately after the termination of HIFU procedure in order to prevent the significant post-operative pain, and that two syringe pumps are needed to deliver the two drugs.

Here are the dosing plans of the regimens mentioned. They may serve as references if the anesthetists do not know the difference of sedation and analgesia requirements between focused ultrasound ablation and other operations. Please remind the anesthetists that the ultimate goal of sedation is keeping the patient in depth at Ramsay Score 3 or 4.

During the HIFU ablation, beside the sedative and analgesic effect of drugs, other non-drug factors including light, communication methods, noise in the surrounding environment, and water temperature should also be controlled, as women are more sensitive to these stimuli.

IV. Risks and Complications of Sedation and Analgesia: Management and Prevention

Last but not the least, we are going to learn the risks and complications of sedation and analgesia and the corresponding management and prevention.

The primary risk associated with sedation and analgesia is respiratory depression. Diagnosis and management of respiratory depression involve identification of possible risks and corresponding prevention.

Patients suffering from respiratory depression may show any of the following signs. First, the patient breathes slowly with respiration rate fewer than 12 times per minute. Second, spontaneous breathing stops for more than 15 seconds. Third, the blood-oxygen saturation changes as a result of the first two conditions. When the blood-oxygen saturation is lower than 90%, the patient has hypoxemia. To prevent the occurrence of



hypoxemia or reduce the difficulty in the management and treatment of hypoxemia, it is necessary to take intervention measures when the patient shows either of the first and second signs before the blood-oxygen saturation decreases to lower than 90%.

So for the management of respiratory depression during treatment, the key is to observe the patient's vital signs, especially the respiration. First, stimulate or encourage the patient to take deep breaths by patting her back to wake her up or increasing the treatment intensity. In the meanwhile, increase the oxygen supply rate for more oxygen uptake. For some snoring patients who cannot maintain smooth ventilation, they can be assisted to hold up their jaws open and unobstructed. For patients in deep sedation who cannot be waken up or maintain spontaneous respiration, administration of antagonist should be considered. For administration of antagonists, please see the slide for details.

The causes of respiratory depression include overdosing, misdilution of drugs, and incorrect evaluation of patient's airway patency. First, overdosing. When patient feels discomfort, additional dose of drugs may be blindly given to improve the analgesic effect. Therefore, to prevent respiratory depression, the repeat dose must be small.

Second, misdilution of drug may happen when the drug is mistaken, resulting in overdosing. Therefore, careful checking should be emphasized, as any negligence may result in a medical accident.

Third, the patient's airway is obstructed. When the patient suffers from respiratory depression due to overdosing, the tongue will obstruct the air getting into the respiratory tract. Thus, pre-treatment evaluation of patient is critical.

Once again, pre-treatment evaluation, preparation of drugs, manual ventilator, and suction catheter in the HIFU theater are all aimed at improving the success rate of rescue should emergencies occur, even though the risk is extremely low. The operator and nurses must double check the drugs to be given, including drug name and dilution method. Patient's consciousness and the sedation depth should be continuously monitored and assessed.