Pearls and Nuances in Vagal Nerve Stimulator Implantation Surgery

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Abstract

Vagal nerve stimulation (VNS) is a proven effective modality of treatment for drug refractory epilepsy and major depression. Recently, the indications have been expanded to various other non-neural indications. The key to a successful surgery includes identification of the vagus nerve and proper application of the device. Meticulous dissection and proper handling of the nerve leads to maximizing therapeutic effect and minimizing complications. In the current article, we describe the technical aspects of performing VNS, focusing on the anatomical variants and intraoperative adjuncts to identify the vagus nerve accurately.

Keywords
- Epilepsy
- Depression
- Heart Failure
- Angina Pectoris
- VNS

Introduction

The vagus nerve is composed predominantly of parasympathetic nerves. It forms the part of the extensive autonomic network that not only supplies the heart, lungs and abdominal visceral organs but also modulates their functions.[1] James L. Cornig was first to report that antiepileptic effects of vagal nerve stimulation (VNS).[2] VNS got momentum when Zabara demonstrated antiepileptic effect in dogs in 1988.[3-5] The first human study was conducted by Penry and Dean. This study reported significant seizure reduction in 50% of patients. VNS is Food and Drugs Administration (FDA)-approved for drug refractory epilepsy (1997) and treatment resistant depression (2005). VNS is increasingly employed for other indications such as chronic headache, rheumatoid arthritis, Chron's disease, heart failure, angina pectoris, and peripheral arterial diseases.

Mechanisms of Action of VNS

Antiepileptic and antidepressive effects of VNS are mediated through nucleus tractus solitarius and dorsal vagal motor nucleus and their connections with central autonomic networks.[4] Biochemical studies showed that there is increase in cerebral metabolites such as gamma-aminobutyric acid (GABA) and serotonin, and these are well correlated with therapeutic effects. Use of VNS in inflammatory conditions such as sepsis and Chron's disease is mediated by vagal anti-inflammatory effects through two pathways: first, increase in adrenocorticotropic hormone (ACTH) and cortisol through modulation of hypothalamic-pituitary-adrenal (HPA) axis; second, through inhibition of production of proinflammatory cytokines such as interleukin-1 (IL-1), IL-6 and tumor necrosis factor (TNF)-α. Indications of VNS are tabulated in ►**Table 1**.

Contraindications

There is no absolute contraindication for VNS, except when it is completely damaged by previous trauma or surgery. Relative contraindications include: 1) radiation therapy to neck 2) left carotid endarterectomy 3) active peptic ulcer disease 4) moderate-to-severe chronic obstructive

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Table 1 Shows various indications for VNS implantation

Indications for VNS
1. Drug refractory epilepsy
a. Focal localization related epilepsy
b. Idiopathic generalized epilepsy
c. Symptomatic generalized epilepsy
d. Failed resection/disconnection surgery
2. Treatment resistant depression
3. Chronic pain
4. Rheumatoid arthritis
5. Sepsis
6. Crohn's disease
7. Heart failure
8. Unresponsive angina
9. Peripheral vascular disease
10. Headache
a. Chronic cluster headache
b. Migraine
c. SUNCT
d. Paroxysmal hemicrania
11. For improvement of consciousness

Abbreviations: SUNCT, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing; VNS, vagus nerve stimulation.

pulmonary disease (COPD) 5) professional singers 6) presence of right vocal cord palsy.

Anatomical Aspects of Vagus Nerve

Vagus is the most extensively distributed cranial nerve which supplies pharynx, larynx, and thoracic and abdominal viscera till right two-thirds of transverse colon. It is composed of approximately 35000 myelinated fibers and approximately 4500 unmyelinated nerve fibers. The nerve arises from medulla in a groove between olive and inferior cerebellar peduncle. After its origin, the vagus traverses through the cerebellopontine cistern and enters the jugular canal along with glossopharyngeal nerve and exits the skull through the jugular foramen superficial to internal jugular vein (IJV). Just inferior to jugular foramen lie superior and inferior nodose ganglia. Intracranial meningeal branches supply dura of posterior fossa. Auricular branch is the first extracranial branch, arising from the vagus in the jugular canal, which carries sensory information from the outer ear. Pharyngeal branch arises, as the vagus exits the foramen supplying muscles of the palate and pharynx.[1] The superior laryngeal nerve (SLN) branches off from the vagus just inferior to the jugular foramen and divides into internal and external branches, running posterior to the internal and external carotid arteries (ICA/ECA). The SLN supplies the larynx at the level of hyoid bone.[1] The vagus then courses between common carotid artery (CCA) or ICA and IJV. As it courses in the rostral to caudal direction, the position of the vagus nerve changes from posterolateral to anterior aspect of carotid artery. Superior and inferior cardiac branches arise at the root of neck, and left recurrent laryngeal nerve loops around arch of aorta and travels in tracheoesophageal groove before supplying larynx.[1]

Surgical implantation of VNS device is a seemingly straightforward procedure, as cervical vagal nerve branching in carotid sheath has previously been shown to be extremely rare. Even with successful implantation, VNS fails in approximately 25% of patients, and undesirable side effects such as dyspnea, hoarseness of voice, cough and throat pain were reported in 17% of patients. Recent literature showed that branching of cervical vagus nerve is much more common than previously thought and this could result in erroneous placement of VNS device at locations other than the main vagal trunk. Hence, knowledge about anatomical variations of the vagus nerve is imperative.

Anatomical Variations of Vagus Nerve

Normal course

Vagus nerve usually courses in the groove between carotid artery and IJV. It lies posterolateral to carotid artery in the upper neck and becomes more anterior or anterolateral to carotid artery in the lower neck. During this course, the vagus nerve does not have branches in the middle and lower cervical region.

Medial course

In this variation, the vagus nerve lies medial to carotid artery in close proximity to the thyroid gland. Vagal nerve identification is challenging, and one must be cognizant of this anatomical variant. This might lead to erroneous placement of the stimulator over the branches other than the main vagal trunk, leading to a therapeutic failure subsequently.

Anterior course

Instead of progressive superficial course of vagus nerve in craniocaudal direction, it lies anterior to the carotid artery. High risk of injury to the vagus nerve exists during dissection if one is not careful and aware of this variation.

Branching Pattern of Vagus Nerve

Branching of left vagus nerve in carotid sheath is less common than the right side (12% vs. 22%). These branches extend inferior to larynx till thorax. This branching is observed between fourth and fifth cervical vertebrae on left side and second and fifth cervical vertebrae on right side. Larger diameters and cross-sections are found in vagus nerve without branching. Cervical vagal branches may be erroneously attributed as main trunk or mistakenly transected during VNS device implantation, and this may contribute to decreased efficacy or occurrence of complications.

Adjuncts for Vagal Nerve Identification

Accurate identification of the vagus nerve is important for successful placement of VNS device. Course and branching pattern of the vagus nerve can be studied by preoperative ultrasonography of the neck. Position of the vagus nerve in relation to the carotid artery and IJV can be studied.

Intraoperative confirmation of the vagal nerve can be accomplished by recording the electromyography (EMG) activity of the vocal cord muscles through endotracheal tube electrodes. Branches of ansa cervicalis may be identified by recording EMG activity from sternocleidomastoid (SCM), genioglossus, sternohyoid, and trapezius.

Surgical Procedure

Preoperative Workup and Counselling

Comprehensive evaluation and proof of disease refractoriness to medical therapy prior to implanting the VNS device is mandatory. Preoperative status of vocal cord status must be assessed by indirect laryngoscopy. History of significant trauma to neck or surgery must be ruled out. Detailed preoperative counselling regarding the need, benefits, and complications prior to surgical implantation of the VNS device is of paramount importance. The need for regular follow-ups and the need for multiple reprogramming of the device should be explained to the caregivers. Approximately, there is 50% reduction in seizure frequency in 50% of patients over a 2-year period. Similarly, 40% response rate and 17% remission rate has been reported in treatment resistant depression as per the current literature.

Surgical Technique

Position

Under general anesthesia, patient is positioned supine with a roll under both shoulders to facilitate neck extension. Head is turned to right side for 30°. This facilitates easy tunnelling. However, head can be kept in neutral position for better anatomical landmarks. Adequate muscle relaxation helps in easy retraction of SCM. Muscle relaxants should be avoided during VNS implantation surgery, if EMG of the vocal cords is planned. The surgical steps are summarized in the ►**Fig. 1**.

Incision

A horizontal skin crease cervical incision, midway between the chin and suprasternal notch or midway between mastoid tip and insertion of SCM, extending between midline and anterior border of SCM is marked. This location of incision has the following advantages: 1) This portion of cervical vagus nerve has less branching; 2) avoids SLN in the upper neck 3); avoids cardiac branches in the lower neck; 4) vagus nerve is more superficial than in the upper neck; and 5) avoids inferior belly of omohyoid in the line of dissection. A 5 cm linear incision for battery placement can be marked at 3 to 4 cm below the clavicle. In lean or malnourished children or adults, this incision can be marked at anterior axillary fold to create subpectoral pouch.

Cervical Dissection

After skin incision, the platysma is cut sharply with scissors. Subplatysmal dissection is done in cranial and caudal direction, so as to facilitate a wider exposure. Deep cervical fascia is divided, inferior belly of omohyoid is retracted medially and SCM is retracted laterally. Dissection is continued medial to SCM under microscope. Bleeding is minimum if dissection is continued in anatomical and avascular plane. Sharp dissection with magnification under microscope provides better anatomical details. Blunt dissection may cause vessel injury, unwanted bleeding, and injury to ansa cervicalis.

Carotid Sheath Dissection

The carotid sheath is opened with sharp dissection using microscissors. Opening of carotid sheath should continue from caudal to cranial direction, as vagus nerve lies more superficial at lower end. However, care must be taken to avoid injury to main trunk or branches. Anatomical variations, discussed earlier, must be borne in mind while exploring the vagus nerve. Ansa cervicalis must be preserved. At least 3 cm length of the vagus nerve is isolated from the surrounding tissues, using atraumatic vascular forceps during dissection. Vascular loop can be used to mobilize vagus nerve during dissection. Vocal cord EMG may be used to confirm the vagus nerve in case of doubts. Extreme caution must be advocated to identify and treat any asystole during the stimulation.

Creation of Subcutaneous Pouch for IPG

Subcutaneous pouch is created in left infraclavicular area or under anterior axillary fold, based on patient's body habitus and preference. It is better to place battery in subpectoral region in case of children. A 5 to 6 cm linear incision is given and subcutaneous pouch is created. Size of the pouch depends on model of VNS being used. Newer models are small and subcutaneous pouch can be small. A too shallow pouch can result in skin necrosis with subsequent exposure of the device. Deeper pouches can pose problem in communicating and programming of the device. Adequate hemostasis must be ensured prior to device placement.

Tunneling

Tunnelling should be done slowly without undue pressure in craniocaudal direction to avoid injury to neck structures. The tunneller is malleable and may be bent appropriately, depending on the position of head. Tunneling should be below lower end of SCM and omohyoid and above clavicle. Once infraclavicular pouch is reached, stylet is removed, leaving the sheath in situ. The caudal end of lead is attached to the sheath and pulled down into the subcutaneous pouch. An appropriate length of lead is pulled down, so as to keep the electrode coils in the vicinity of the dissected part of the vagus nerve (►**Fig. 1**).

Wrapping of Electrode Around the Vagus Nerve

The cranial end of lead consists of three coils. The caudal most coil is anchor tether. The middle and cranial coils have

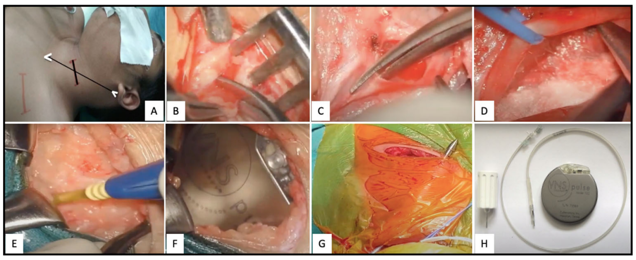

Fig. 1 Illustrates main surgical steps involved vagus nerve stimulation (VNS) implantation. (**A**) Shows position of patient and site of left cervical and infraclavicular incisions. (**B**) A 5 cm linear incision and cutting of platysma sharply helps in better cosmesis during wound healing. (**C**) Sternocleidomastoid (SCM) and inferior belly of omohyoid are retracted and carotid sheath is being opened by sharp dissection. (**D**) Vagus nerve is looped using vascular loop and a length of 3 cm is freed from surround connective tissue (epineurium is intact). (**E**) Infraclavicular incision is made and pouch for implantable pulse generator (IPG) is being created. (**F**) Adequacy of subcutaneous pouch is being checked. (**G**) Tunnelling is made using tunneller provided with VNS device. (**H**) Shows requirements of VNS device implantation—IPG, lead and hex screwdriver.

positive and negative polarity, respectively. Positive electrode has white suture embedded in the coil, whereas the anchor tether and the negative coils have green suture. As mean diameter of vagus nerve is 3 mm, coils with internal diameter of 3 mm are commonly used. The coils are wrapped around the vagus nerve from below upward. Keeping the cranial end of the lead posterior to vagus nerve, the coils are stretched completely, holding sutures parallel to the nerve trunk and then released. The coils get wrapped around the nerve trunk easily with this maneuver. Minor adjustments can be done if not applied properly. Handling of vagus nerve should be gentle to avoid injury and subsequent scarring. Proper wrapping of electrodes around the nerve must be ensured. Coils must be reapplied if there is space between the nerve and the coils or if it is too tight. Any hematoma between coils and nerve must be cleared.

IPG Placement

The lower end of lead must be cleaned with dry gauze or cotton soaked in sterile water to clean the blood. Normal saline should not be used, as it can conduct current, leading to implantable pulse generator (IPG) damage. The lower end of the lead is inserted in the receptacle port of IPG appropriately. Once lead in inserted, the setscrew is tightened with hex screw driver till clicks are audible. When properly assembled, the outer ring of lead is inside the generator and provides water-seal apposition to the assembly. Once lead-IPG assembly is done and placed in subcutaneous pouch, completeness of the circuit must be checked with a programming wand. The impedance should be in the range of 700 to 1400 Ω. If the impedance is high, coils must be checked if they are very loose or there is hematoma around nerve trunk or blood or debris around lower end of the lead. If the problem still persists, generator diagnostics are employed with the resistor assembly. If IPG is normal and problem persists, change the lead and perform diagnostics. If the assembly is found complete, strain loop must be made in cervical region.

Strain-Free Loops

It is important to avoid strain over the nerve by the lead, maintain anchorage of the lead for the therapeutic effect of VNS, and avoid complications. Creating strain-free loops ensures that position of coils is unaffected during neck movements or fidgeting of IPG. Appropriate length of lead is pulled into cervical incision to make two loops. The loops are anchored to fascial structures using ties. Loops are not anchored to muscles, as it may cause movement when SCM or other muscles contract.

Once tension-free loops are created and anchored to fascia, deep cervical facia is closed. Platysma is sutured back using absorbable suture (3–0). Skin is closed in layers. The extra length of lead is looped behind the IPG and placed in the subcutaneous pouch. This will avoid inadvertent damage to lead in case of reexploration. The subcutaneous pouch is closed in layers after achieving hemostasis. A final diagnostic run is performed to check completeness of circuit and impedance. If the assembly is found complete, dressing can be done and patient can be extubated.

Programming of Device

The aims of programming are as follows: control seizure, and minimize stimulation-related side effects with minimal possible settings. We routinely follow device programming after 7 to 10 days after surgery. Programming is started with a current of 1 mA, frequency: 20 or 30 Hz, pulse width of 125 or 250 or 500 microseconds, ON-time of 30 seconds, and OFF-time of 5 minutes of duty cycle. This 10% duty cycle provides battery life of 10 years. The current can be increased in increments of 0.25 mA. With newer model Sentiva 1000, it is possible to adjust current in increments of 0.125 mA and preprogram subsequent changes to occur at preset intervals. This is particularly useful for patients from remote locations. Patient is also provided with a magnet, which can be used to terminate an event in case of aura. The current of magnet is usually set 0.25 mA higher than IPG settings (►**Fig. 2**).

Complications

Related to Surgery

Patient must be watched for respiratory distress, following surgery, which can be due to hematoma formation, as in thyroid surgery. Vagal nerve damage can cause permanent hoarseness of voice, dyspnea, dysphagia, and unilateral vocal cord palsy. Hence, vagus must be minimally handled during surgery, and its vascularity should be preserved. Blunt dissection can result in injury of ansa cervicalis. Major vascular injury is rare. Superficial surgical site infections are rarely documented and easily treated with antibiotics. Deep infections requiring lead explantation can occur in 1% of patients.

Related to Device

Coils must be tension-free, and appropriate tension-free loops are created. Appropriate size of IPG must be selected to minimize skin necrosis. Children can fiddle with IPG, and twisting of lead may occur, which will result in lead fractures,

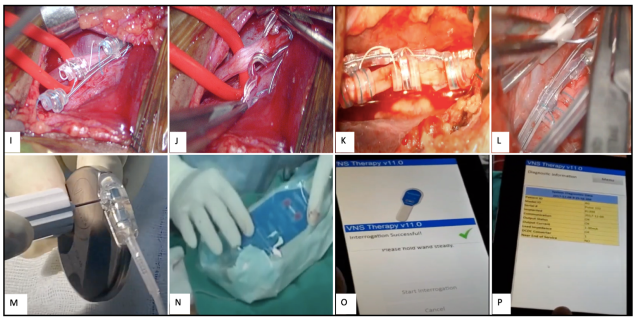

Fig. 2 (**I**) Proximal end of lead and coils—anchor and negative coils are embedded with blue sutures and positive coil is denoted with white suture. (**J**) The lead lies parallel and posterior to vagus nerve, and coil is stretched parallel to nerve, so that when released, it will easily get wrapped around nerve by elastic property. Minor adjustments may be needed sometimes. (**K**) Wrapping of all coils around nerve and final position of lead and coils can be seen. Ensure that no hematoma lies around vagus nerve. (**L**) Preparing and suturing of strain-free loops to fascia. (**M**) Connecting lower end of lead to implantable pulse generator (IPG). Ensure that lead is inserted till metal contact is completely inside and watertight seal is achieved. Tightening of screw using hex screwdriver till two clicks are heard. (**N**) Placing of programming wand over the device and running device diagnostics. (**O**) Programming device shows diagnostics are successful. (**P**) Shows final result of diagnostic test and impedance is found to be fine, which means circuit is intact.

snapping from vagus nerve, and therapeutic failure. Lead fracture can occur with growth spurt, which can result in neck pain and therapeutic failure. In case of lead fracture and need for revision, coils must be separated after cutting them as close to vagus nerve as possible and avoid nerve damage.

Related to Stimulation

Side effects related to stimulation result during programming and usually subside with time. Common stimulation-related side effects include hoarseness (immediate 30%, improve to 2% with time), dysphagia, cough, breathlessness, and feeling of tingling sensation in throat. Often, these side effects can be circumvented by modifying stimulation parameters. Lowering current or frequency can decrease hoarseness, and decreasing pulse width can decrease pain in the throat (2.8%). Sometimes, adjusting duty cycles to shorter ON/OFF cycle can help in managing these complications. Hypersalivation related to stimulation is self-limiting. If it is not controlled with parameter adjustment, glycopyrrolate can be of help.

Conflict of Interest
None declared.

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Note: Reference 6-24 is available online

