Epilepsy & Behavior Reports 15 (2021) 100437

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr

Surgical revision after Vagus Nerve Stimulation. A case series

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ARTICLE INFO

Article history:
Received 5 December 2020
Revised 26 February 2021
Accepted 4 March 2021
Available online 26 March 2021

Keywords:
Epilepsy surgery
Revision surgery
VNS

ABSTRACT

With increasing use of vagus nerve stimulation (VNS) as an adjunct treatment for drug-resistant epilepsy, revision surgery of VNS grows in importance. Indications for revision surgery are diverse and extend of surgery varies. We report a retrospective review on indications and complications of VNS revision surgery at our center. Of 90 VNS procedures 54.4% were revision surgeries. Among those the vast majority was due to depletion of the battery. The entire system was explanted in 15 patients, due to no beneficial effect detected (n = 4), due to irritating side effects (n = 4), and so further diagnostics could cbe carried out (n = 7). Interestingly in three of the patients who underwent further diagnostics, resective epilepsy surgery was performed. Surgical complications occurred in 8.2%. In our experience, revision surgery of VNS was a frequent and safe procedure. There is a need to carefully reviewthe initial indication for VNS implantation prior to revision surgery.

Introduction

According to World Health Organization (WHO) ~50 million people worldwide suffer from epilepsy, making it one of the most common neurological diseases [1]. Approximately 30% of those patients remain multi-drug resistant. Of those ~15 million patients 30% might be suitable for resective epilepsy surgery with a success rate of 58–77% [2–4]. The remaining patients who do not benefit from resective epilepsy surgery, plus another 30% of the drug-resistant patients who are not eligible for resective epilepsy surgery (summarized ~4.5 million) remain candidates for neuromodulation-therapies such as vagus nerve stimulation (VNS) [1,5,6]. VNS was approved in the European Union (EU) in 1994 for use as an adjunctive therapy for reducing partial seizures (with or without secondary generalization) or generalized seizures, which are resistent to antiseizure medication. With a rising number of implanted devices, revision surgery grows in it's importance. Indications for revision surgery are diverse: depletion of the battery, high impedance or breakage of the lead, mechanical irritation and discomfort through the implanted device, infection, lack of effectiveness or further MR-diagnostics that require explantation of the VNS-System in case MRI is needed within the exclusion zone of the respective VNS model [7]. The VNS device consists of a battery that is implanted in a subcutaneous pocket below the clavicle and a bipolar electrode that is wrapped around the left vagus nerve [8]. Over time, the helical electrode coils become encapsulated by extensive scar tissue, which may potentially cause a high impedance resulting in malfunction. on the one hand and makes complete electrode removal challenging on the other hand [9]. Revision surgery does not always comprise generator and electrode revision, so complication rates might very substantially depend on the extent of the operation. We report our experience and complications from VNS revision surgery.

Methods

At our center all epilepsy surgeries have been prospectively enrolled in a database since 2013. In a computerized search using diagnostic and procedural codes patients who underwent VNS procedures between 2013 and 2020 were identified. The following models were used: Pulse® Generator – Model 102, Pulse Duo® Generator – Model 102R, Deimpulse® Generator – Model 103, Aspire HC® Generator – Model 105, Aspire SR® Generator – Model 1006, SenTiva® Generator – Model 1000. Primary VNS implantations were excluded from the study. All remaining cases were defined as revisions and included in the retrospective analysis. Indications and complications were systematically recorded. The study was conducted in accordance with the Declaration of Helsinki. IRB approval was not required since the data was collected as part of the routine clinical procedure.

Results

Among 469 surgical procedures (175 resective procedures, 204 diagnostic procedures including intracranial depth electrodes, subdural strip and subdural grid electrodes and foramen-ovale

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https://doi.org/10.1016/j.ebr.2021.100437
2589-9864/

electrodes, peg- and foramen-ovale), a total of 90 left side VNS procedures were found, all performed by a single surgeon. Of these, 49 (54.4%) were revision surgeries. None of the VNS patients had previous resective surgery. Four patients had a former battery replacement due to depletion of the battery and one patient had invasive diagnostic without consecutive resective surgery. Patients' median age (±SD) was 38 (±13.1) years (m/f/d: 25/24/0). As expected, the majority of cases were due to depletion of the battery (n = 34). In 30 patients only the battery was revised, while in 4 patients the electrode was revised too. All 34 patients underwent reimplantation. Median time from initial implantation to replacement was 8.5 (±2.5; variance ± 6.0) years (Fig. 1A). Replacement was performed when battery status reached end of service (EOS), or rarely when patients were unable unto meet an appointment in the outpatient department for more than six months. Since the battery status was regularly checked, clinical EOS (i.e. increase or change in seizure pattern, painful stimulation, behavioral worsening) [10] did not occur in the patients who underwent revision due to battery status. There were no differences regarding depletion of the battery between various VNS models. The entire system was explanted in 15 patients, since no positive effect was detectable (four patients), due to irritating side effects (four patients) or because further diagnostics should be carried out (seven patients) (Fig. 1B). None of these patients underwent reimplantation. None of the four patients with irritating side effects demonstrated decreased battery status, so clinical EOS was less likely [10]. In three of the patients who underwent further invasive diagnostics resective epilepsy surgery was performed. In four of 49 interventions direct surgical complications occurred: one subcutaneous hematoma, two transient recurrent laryngeal nerve palsies and one bleeding from an injury of the jugular vein. In the latter case, there was minimal blood loss, which was stopped intraoperatively by a single suture (Fig. 2). Revision of the electrodes was not associated with higher risk of complications, than revision of the generator alone in our series.

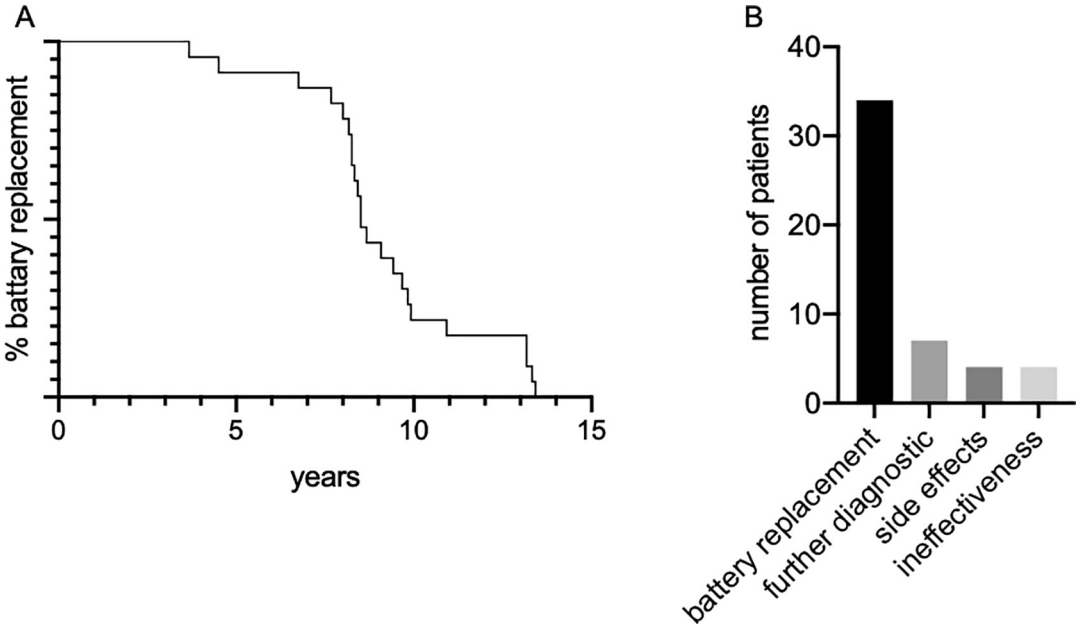

Fig. 1. A) Kaplan-Meier estimator for battery exhaustion. Median time to replacement was 8.5 (±2.5) years, n = 23. B) Indications for revision surgery: Battery replacement 34, further diagnostics 7, side effects 4, ineffectiveness 4.

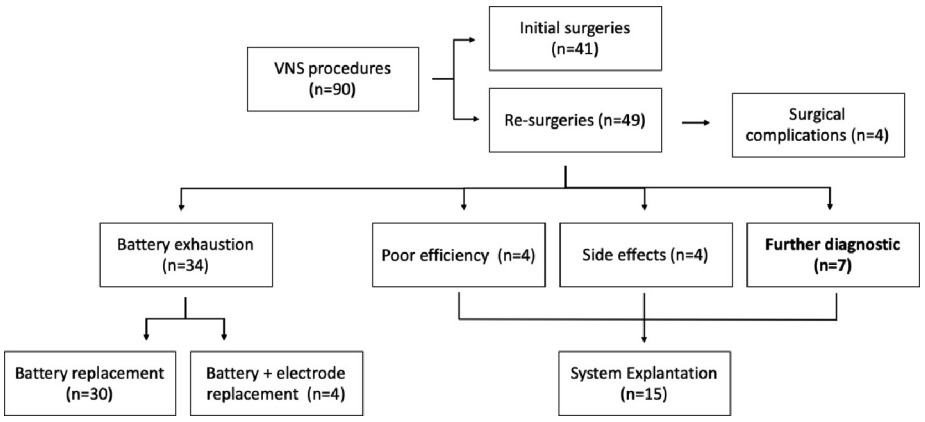

Fig. 2. Flowchart regarding indications for revision surgeries and according procedures. Remarkably seven of 15 patient who underwent explantation of the entire system underwent further diagnostics.

Table 1
Literature overview. Original studies describing removal or revision of the (partial) VNS-System. VNS = Vagus Nerve Stimulation.

Study	Type of Study	No. of patients	Indication for Revision	Surgical Complications
Agarwal et al. (2011)	Retrospective case series (Revision of VNS electrodes)	23 (children)	Device malfunction High lead impedance (n = 20) Symptoms Infection (n = 3)	None
Dlouhy et al. (2012)	Retrospective case series (VNS lead revision surgery)	24 (23 adults)	Device malfunction High lead impedance (n = 18) Short circuit (n = 2) Symptoms Ineffectiveness (n = 18) Side effects (n = 4)	Tauted lead cable (n = 1)
Waseem et al. (2014)	Retrospective case series (Lead revision surgery)	10	Device malfunction Lead breakage (n = 8) Dislodged electrode (n = 1) Iatrogenic intraOP lead disruption (n = 1) Symptoms N/A	N/A
Couch et al. (2015)	Retrospective case series (Battery replacement and revision surgery)	348	Device malfunction Battery replacement (n = 235) High impedance (n = 53) Symptoms Ineffectiveness (n = 61) Further diagnostic (n = 45) Infection (n = 12)	N/A
Aalbers et al. (2015)	Retrospective case series (Removal or replacement of VNS system)	35 (25 adults)	Device malfunction Lead damage (n = 2) Symptoms Ineffectiveness (n = 19) Further diagnostics (n = 5) Side effects (n = 3)	Laceration of jugular vein (n = 2) Vocal cord paralysis (n = 1)
Champeaux et al. (2017)	Retrospective case series (Removal or replacement of (partial) VNS-System)	41 Lead (n = 6) VNS-System (n = 35)	Device malfunction Lead damage (n = 11) Symptoms Ineffectiveness (n = 22) Infection (n = 1)	None
Gigliotti et al. (2018)	Retrospective case series (Revision or Removal of VNS System)	32	Device malfunction High lead impedance (n = 12) Lead damage (n = 4) Symptoms Ineffectiveness (n = 5)	Infection (n = 4) Hematoma (n = 1)

Discussion

With increasing number of VNS procedures that are performed, reports about revision surgery becomes increasingly important. We describe our collective experience of 49 revision surgeries performed for different reasons. Our data show that revision surgery was a frequent, however safe procedure. The rate of complications was relatively low with four surgical complications among 49 procedures (i.e. 8.2%), none of which lead to permanent sequelae. Bleeding from the jugular vein occurred in one case due to a laceration. While this has to be interpreted as serious complication of an elective procedure, it was brought under control quickly without harm. We found VNS to be a well-tolerated long-term treatment option with a median of 8.5 (±2.5) years durability of a single battery. It remains interesting that 7 of 15 patients in our study who had their entire systems explanted underwent further epilepsy diagnostics, showing that the initial indication might have retrospectively not been correct. There are several retrospective single center studies which report different aspects of revision surgery [11–17]. Couch et al. (2015) report an average time to replacement of the battery of 4.9 (range 0.2–12) years which is remarkably shorter than in our cohort. In our data only first battery replacements were collected, while in the data of Couch et al. 24.7% battery replacements were at least second replacements [14]. This finding is in accordance with studies about other types of neurostimulators (i.e. implantable pulse generators for deep brain stimulation) which report longest battery longevity of the first device [18]. In other studies, battery replacements are not taken into account, since it is considered routine maintenance. Regarding indication for revision surgery various studies focus on either malfunction of the device or patient's symptoms that lead to revision surgery. Among those reasons, ineffectiveness is most common (26% range 15–75%) [12,14–17]. Concerning malfunctions of the device high lead impedance and lead breakage are discussed as main indication for revision [11–17]. All studies come to conclusion that in spite of certain complications, VNS is a well-tolerated adjunct treatment for drug-resistant epilepsy. An overview of the literature is provided in Table 1. Our data are in accordance with those previously published studies and underline an acceptable complication profile and satisfactory long-term treatment. On the other hand, 7 of 15 patients who underwent further epilepsy diagnostics indicate nearly 50% recommended initial treatment with VNS, a palliative decision since resective epilepsy surgery offers a greater likelihood of seizure freedom [2,19,20]. In contrast to recent studies in which a majority of patients had resective epilepsy surgery prior to VNS [21–23] none of the patients we report underwent resective surgery beforehand. This might be explained by a site-specific limitation of our study: Since our institution cooperates with specialized care facilities most our patients who are evaluated for VNS are severely disabled with multifocal seizure origin and therefore not eligible for resective epilepsy surgery.

Conclusion

Our data emphasize the need to carefully revisit the initial indication for VNS prior to revision. Implantation of a VNS-System should not be carried out until a reasonable pre-operative investigation and adequate discussion of all possible treatment options has been conducted. Multiple VNS surgeries (i.e. revision) are commonplace in the postoperative course of VNS patients. The rate of major complications of VNS revision surgery is acceptablely low. In our cohort, lead revision was not associated with higher risk of complications, than revision of the system or the generator alone. We suggest that when a clear indication for VNS is present, the high likelihood of subsequent surgeries should be considered but not preclude recommendations to pursue VNS.

Ethical standard

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants and/or their legal representatives included in the study according chapter 3, Art. 13 of the General Data Protecion Regulation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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