biomedicines

MDPI

Review

Neuromodulation of the Cardiac Autonomic Nervous System for Arrhythmia Treatment

Benjamin Wong [1,2,†], Yuki Kuwabara [1,†] and Siamak Salavatian [1,2,3,*]

[1] Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh, Pittsburgh, PA 15261, USA
[2] Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA 15219, USA
[3] Department of Medicine, Division of Cardiology, University of Pittsburgh, Pittsburgh, PA 15213, USA
* Correspondence: salavatian@pitt.edu
† These authors contributed equally to this work.

Abstract

This review explores current and emerging neuromodulation techniques targeting the cardiac autonomic nervous system for the treatment and prevention of atrial and ventricular arrhythmias. Arrhythmias remain a significant cause of morbidity and mortality, with the autonomic nervous system playing a crucial role in arrhythmogenesis. Interventions span surgical, pharmacological, and bioelectronic methods. We discuss the range of neuromodulation methods targeting the stellate ganglion, the spinal region, the parasympathetic system, and other promising methods. These include stellate ganglion block, stellate ganglion ablation, cardiac sympathetic denervation, subcutaneous electrical stimulation, thoracic epidural anesthesia, spinal cord stimulation, dorsal root ganglion stimulation, vagus nerve stimulation, baroreflex activation therapy, carotid body ablation, renal denervation, ganglionated plexi ablation, acupuncture, and transcutaneous magnetic stimulation. Both preclinical and clinical studies are presented as evidence for arrhythmia management.

Keywords: neuromodulation; atrial arrhythmias; ventricular arrhythmias

check for updates

Academic Editor: Anand Prakash Singh

Received: 19 May 2025
Revised: 13 July 2025
Accepted: 18 July 2025
Published: 21 July 2025

Citation: Wong, B.; Kuwabara, Y.; Salavatian, S. Neuromodulation of the Cardiac Autonomic Nervous System for Arrhythmia Treatment. *Biomedicines* **2025**, *13*, 1776. https://doi.org/10.3390/biomedicines13071776

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Cardiac arrhythmias, both atrial and ventricular, affect millions and remain a leading cause of morbidity and mortality worldwide. Atrial fibrillation (AF) accounts for more than half of all arrhythmia cases, currently affecting over 2.2 million individuals in the United States, a number projected to rise to approximately 5.6 million by 2050 [1]. AF significantly increases the risk of stroke, imposing a substantial burden on the healthcare system [2]. On the other hand, ventricular arrhythmias (VAs) are the leading cause of sudden cardiac death, responsible for an estimated 180,000 to 250,000 deaths annually in the U.S. [3]. Although current therapies, including antiarrhythmic drugs, rate control agents, and anticoagulants, are widely used, they often have limited efficacy, notable side effects, and fail to provide durable outcomes. Interventional approaches such as catheter ablation and implantable cardioverter-defibrillators (ICDs) offer more effective alternatives but are associated with procedural risks and are not curative, as their long-term effectiveness may diminish over time [4,5].

The cardiac autonomic nervous system (CANS) consists of efferent sympathetic and parasympathetic pathways as well as afferent pathways that regulate heart function. These neural pathways are interlinked in a cardio-neural hierarchy [6–8]. Within this hierarchical structure, afferent and efferent signals from the sympathetic and parasympathetic nervous

systems modulate the heart and vasculature during every cardiac cycle [9,10]. In cardiac disease, including arrhythmias, the activation of afferent/sensory pathways results in sympathoexcitatory and parasympathetic inhibitory reflexes, which are mediated through the CANS hierarchy [11–14]. Several preclinical and clinical studies have shown that sympathetic excitation and/or vagal withdrawal play a crucial role in the pathophysiology of cardiac disease, especially arrhythmia [14–17]. As the imbalance of the CANS is one of the mechanisms in the development and triggering of arrhythmia, modulating the CANS can be a therapeutic option [9,18–20]. Recent meta-analyses have shown the impact of surgical neuromodulation methods used in prior studies to treat cardiac arrhythmias [21]. This review overviews recent preclinical studies and clinical trials in which neuromodulation has been performed to treat atrial or ventricular arrhythmias (Figure 1).

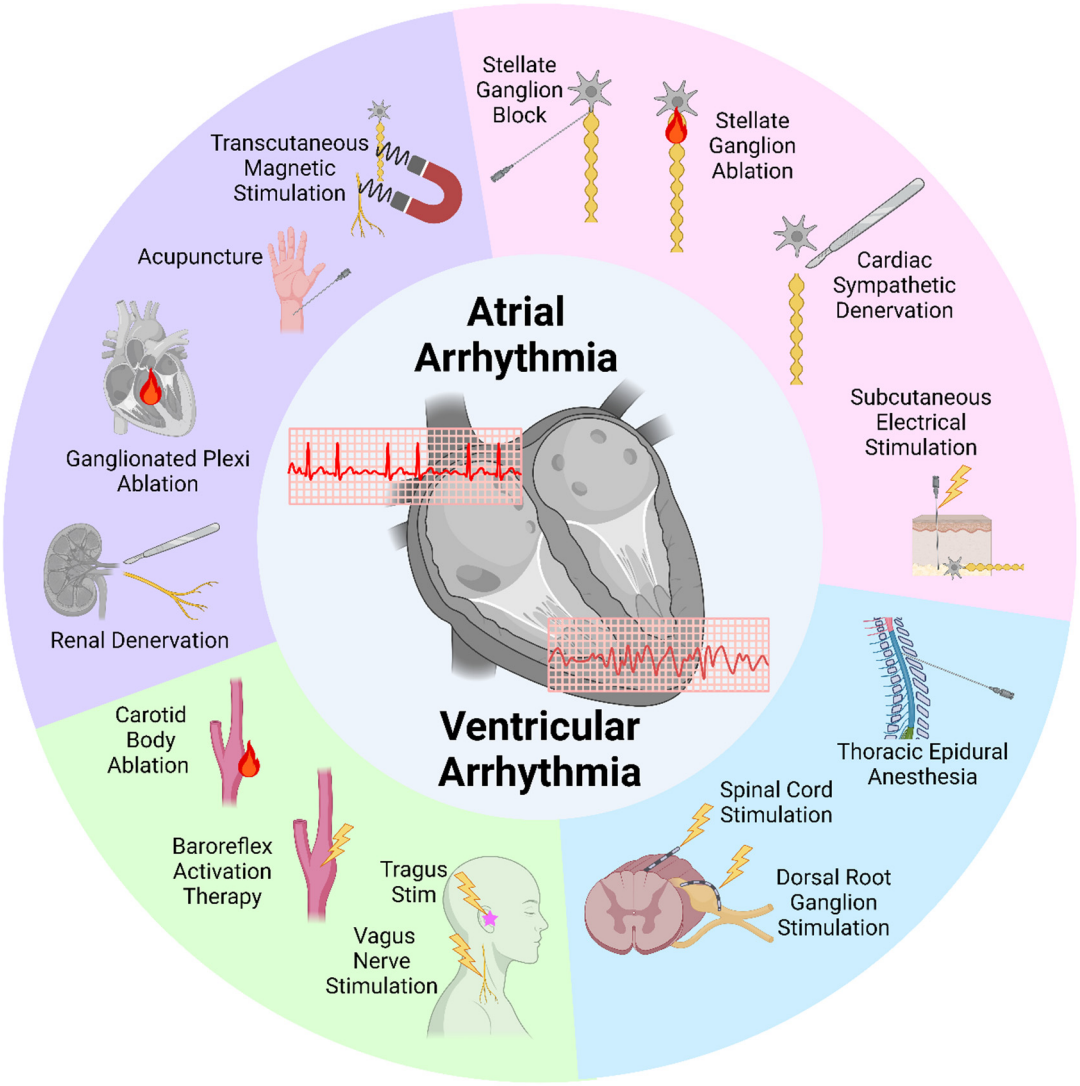


Figure 1. Neuromodulation therapies to treat atrial and ventricular arrhythmias. Therapies range from pharmacological methods to surgical procedures to specialized devices targeting the stellate ganglion (pink), the spinal cord region (blue), the parasympathetic nervous system (green), and other (purple). Created in BioRender. Wong, B. (2025) https://BioRender.com/5kqb43n.

2. Targeting the Stellate Ganglion

2.1. Stellate Ganglion Block

The stellate ganglia (SG) are neural networks located in the lower part of the neck on the sympathetic chain on both sides of the body [22]. The spinal preganglionic sympathetic

neurons synapse with postganglionic neurons in the SG, delivering efferent sympathetic output to the heart muscle [23]. This offers an ideal therapeutic site since the spinal sensory afferents implicated in arrhythmogenesis travel through the SG. The SG block (SGB) can be carried out by infusing anesthetic agents, so the surrounding fibers and possibly neurons can be inhibited and help attenuate both afferent and efferent neurotransmission at the SG. Recent reviews discussed the variety of antiarrhythmic drugs and SGB interventions utilized for electrical storm and VAs [24–27].

For anesthetic agents, bupivacaine, lidocaine, and ropivacaine are mostly used, but injections of toxins, such as botulinum toxin A (BoNT-A), have also been explored for SGB [24,28,29]. Lidocaine exhibits a higher binding affinity for inactivated fast sodium channels; however, its use is limited by time- and dose-dependent neurological side effects [24]. In patients experiencing ventricular arrhythmia storm, SGB using either single-injection or continuous-infusion techniques significantly reduced arrhythmia burden. However, the continuous-infusion approach achieved a greater reduction in arrhythmia episodes, maintained a similar safety profile, and eliminated the need for repeat interventions [30]. While lidocaine is fast-acting, bupivacaine and ropivacaine are long-acting agents [24]. These pharmacokinetic differences allow for strategic combinations to achieve tailored anesthetic effects depending on the desired onset and duration of nerve blockade. BoNT-A and conventional anesthetics differ in onset, duration, and safety. Traditional agents like lidocaine offer rapid but short-term relief (minutes to hours), while BoNT-A has a delayed onset but can last weeks to months [31,32]. Local anesthetics may cause systemic toxicity if misapplied, whereas BoNT-A risks include localized muscle weakness and unintended spread [24,28]. Clinical evidence for BoNT-A in pain or autonomic modulation remains limited. Future SGB studies should directly compare BoNT-A and conventional anesthetics in controlled trials and explore their mechanisms and optimal applications.

Imaging guidance with ultrasound [30,33–35] was introduced as a novel alternative compared to conventional SGB with anatomic landmarks [36]. The standard approach targets the left SG; however, the right SG may be considered in cases of recurrent arrhythmias [26]. Nevertheless, it has been suggested that right SG blockade does not yield additional benefit and may increase the risk of bilateral phrenic nerve paralysis [24].

Early studies on canines showed an increase in ventricular fibrillation (VF) thresholds after SGB [23]. This was then translated to human patients and confirmed [37]. A later rat study showed left SGB lowering arrhythmia scores and even reducing the infarct size [38]. Mechanistically, a study on rabbits posits that left SGB increases the electrophysiological stability of the ventricular myocardium by prolonging 90% of the monophasic action potential duration of the epicardium, decreasing the dispersion of repolarization, and increasing the effective refractory period along with ventricular threshold [39]. They demonstrated that SGB prolonged the atrial effective refractory periods on both the right and left sides of the atria. SGB extensively targets the treatment of VAs. Many clinical case reports have shown the effectiveness of ceasing or reducing episodes of VAs [15,34,40–42]. Meng et al. reviewed the efficacy of the SGB in managing VAs and reported that SGB showed a significant decrease in VA burden and the number of external and implanted defibrillator shocks [43]. After the SGB procedure, 80.6% of patients in the study survived discharge [43]. Another study compared the efficacy of SGB between single and continuous injections in patients with VA storm [30]. The number of sustained VAs within 24 h was significantly reduced with the continuous infusion compared to the one before treatment. More recently, Baldi et al. evaluated the efficacy of preemptive percutaneous SGB for managing electrical storm [44]. They compared one group that received SGB prior to antiarrhythmic drug administration (early SGB) with a group that received it afterward (delayed SGB) [44]. Their findings indicated that early SGB significantly reduced the number of arrhythmic

episodes treated within the first hour, decreased the need for defibrillation, and potentially mitigated the overall incidence of electrical storm [44].

In a recent multicenter study, Savastano et al. (STAR study) reported improved management of VAs in 131 patients following percutaneous SGB [26]. Notably, 106 patients (92%) experienced a reduction in the number of treated arrhythmic episodes [26]. The study did not identify differences between image-guided and anatomical landmark techniques for SGB [26]. Similarly, another multicenter study by Chouairi et al. demonstrated that SGB was associated with a decreased burden of VT/VF and a reduced need for defibrillation [27]. The number of VT/VF episodes significantly declined ($p < 0.001$) within 24 h following SGB [27]. A key limitation of this study was the absence of a control group, highlighting the need for future investigations to evaluate potential placebo effects [27].

Overall, the effect of SGB on atrial arrhythmias (AAs) has not been well-studied, even less so in humans [45]. Leftheriotis et al. investigated the effect of unilateral SGB on the electrophysiology of the atrium and AF induction in paroxysmal AF patients [46]. They found that SGB decreased both AF inducibility and duration [46]. A recent case study by Groenendyk et al. described a 73-year-old woman with rapid AF who received SGB via ropivacaine infusion [47]. After 13 days of hospitalization, her left ventricular ejection fraction improved from approximately 10% to 25% [47]. This represents the first published in-human case reporting the use of SGB for the management of acute AF [47].

2.2. Stellate Ganglion Ablation

As discussed, SG is one of the neuromodulation targets for arrhythmia. The justification of SG ablation is the same as SGB. It can be performed using continuous radiofrequency under fluoroscopic guidance, instead of injecting anesthetic drugs as the SGB [48]. Animal studies show SG ablation prevents VAs induced by myocardial infarction (MI) [49,50]. There are also studies on AAs in dogs showing the potential of SG cryoablation [51]. This involves inserting a cooled catheter into the ablation target to freeze and destroy it [51]. Bilateral SG cryoablation decreased the sympathetic tone and SG nerve activity associated with the onset of AAs [51]. A later study confirmed this and showed that subcutaneous nerve activity can help estimate cardiac sympathetic tone and the effects of cryoablation [51].

There are not many clinical studies targeting SG for ablation. The study by Rao et al. showed that radiofrequency SG ablation treated patients with electrical storm [48]. Bilateral SG ablation was shown to be effective in treating electrical storm, with survival at discharge for all patients at a mean follow-up of 22 $\pm$ 8 months [48].

The potential risks and complications associated with this approach have not been well reported to date. They are presumed to be similar to those of SGB, particularly concerning acute procedural risks and hemodynamic effects. However, long-term outcomes remain uncertain and warrant further research, perhaps by performing prospective trials.

2.3. Cardiac Sympathetic Denervation

It has been widely known that the autonomic nervous system plays a crucial role in the genesis and maintenance of VAs. Cardiac-related preganglionic somas reside within the intermediolateral cell column in the spinal cords; these somas project axons to other postganglionic somas at the stellate, middle cervical, mediastinal, and intrinsic cardiac ganglia [52]. Additionally, these ganglia consist of neural networks with afferent neurons and local neurons in the circuit. These intrathoracic ganglia function within a hierarchy for cardiac control, where peripheral elements are mainly involved in cardio–cardiac reflexes [8]. There is both experimental and clinical justification that fatal arrhythmias can be mitigated by cardiac sympathetic denervation (CSD), especially in the case of augmented sympathetic activity [53–55]. The safety and feasibility of video-assisted thoracoscopic

surgical CSD have been reported, which can provide a minimally invasive approach with minimal perioperative complications [56].

In rats, CSD was shown to reduce the susceptibility of AF by altering the expression of connexin 43, known as a major gap junction protein found in the heart [42]. In patients with a history of AAs, CSD was shown not to change the AAs' burden [57]. While adjunctive therapies are promising, along with CSD [45], more studies need to be conducted to understand the direct impact of CSD on AF in human patients. In terms of VF, many past studies explore the effects of CSD in different models: it has been shown to increase the inducibility threshold of VF, treat QT syndrome, decrease the number of cardiac events, and decrease the number of shocks from preoperative implantable defibrillators [58–60]. A recent review paper summarized similar outcomes, showing a significant reduction in corrected QT (QTc) interval after left CSD (LCSD) with no evidence of arrhythmias and reduced beta-blocker dependence [61]. A study published in 2021 showed a decreased mean QTc interval of 14 long QT syndrome patients from 506.2 ms to 476 ms after CSD, and they concluded bilateral CSD (BCSD) to be an effective and safe treatment [62]. Another report by Bourke et al. showed that among nine patients with LCSD, three patients had complete success with LCSD [63]. A recent review and meta-analysis by Hanna et al. detailed the minimized rate of ICD shocks and occurrence of VAs [64]. Furthermore, Assis et al. reported the effectiveness of BCSD to the burden of ventricular tachyarrhythmias [65]. Freedom from sustained ventricular tachycardia (VT) or ICD shock was 60% and 54.5% after BCSD at 1 and 4 years. A recent study by Ahmed et al. further investigated BCSD as a treatment for VA in patients with prior unsuccessful premature ventricular contraction (PVC) ablation procedures [66]. The study demonstrated that BCSD was associated with significant reductions in PVC burden, improvements in left ventricular ejection fraction, and the discontinuation of antiarrhythmic medications [66].

To compare the effectiveness between LCSD and BCSD after one year, Vaseghi et al. reported the shock-free survival rates from sustained VT/ICD shock among 121 patients who underwent left or bilateral CSD: 58.2% and 50.4%, respectively [67]. CSD reduced the burden of ICD shocks between study entry and follow-up.

Although CSD has demonstrated substantial effectiveness in reducing arrhythmia burden, patient responses remain highly variable. Contributing factors to this heterogeneity include underlying cardiac pathology (e.g., ischemic versus nonischemic cardiomyopathy, channelopathies), severity of heart failure (with advanced New York Heart Association [NYHA] class predicting poorer outcomes), and procedural variations (such as left versus bilateral CSD and the inclusion of Kuntz nerve ablation) (Table 1).

Table 1. Key clinical studies on cardiac sympathetic denervation for refractory ventricular arrhythmias and heart failure.

Study (Year)	Population (n)	Age (Years)	Cardiac Pathology	CSD Approach	Primary Outcomes
Hofferberth et al. [68] (2014)	24	5 weeks to 27 years	Long QT syndrome, catecholaminergic polymorphic VT, idiopathic VT	Left	73% arrhythmia reduction; 55% arrhythmia-free
Vaseghi et al. [67] (2017)	121	55 ± 13	Structural heart disease, refractory VT	Left or bilateral	1-year freedom from VT/ICD shock: 58%; ICD shocks reduced

Table 1. *Cont.*

Study (Year)	Population (n)	Age (Years)	Cardiac Pathology	CSD Approach	Primary Outcomes
Cai et al. [69] (2019)	19	60.3 ± 14.6	Structural heart disease, recurrent VA	Left (14), bilateral (5)	VA/ICD therapies reduced; 3-year heart transplant/death-free: 52.6%
Shah et al. [70] (2019)	173	54.6 ± 2	Structural heart disease, refractory VA	82% bilateral	Event-free: 58–100%; 28% complication rate (mostly minor)
Barwad et al. [71] (2021)	65	50 ± 18	Structural heart disease, refractory VT	Surgical (mostly bilateral)	92% reduction in defibrillation shocks; 2-year ICD shock/death-free: 51.5%
Ertugrul et al. [62] (2021)	14	8–19 years	Long QT syndrome, catecholaminergic polymorphic VT, other	Bilateral + Kuntz ablation	Arrhythmia reduction; no major complications
Yalin et al. [72] (2021)	10	61.6 ± 19.6	Nonischemic cardiomyopathy, r efractory VA	Left (6), bilateral (4)	VA/ICD shocks reduced; 2 deaths (not CSD-related)
König et al. [73] (2022)	21	63.7 ± 14.4	Structural heart disease, refractory VA	90.5% bilateral	77% ICD shock-free at 9 mo; 9.5% major complications
Brady et al. [74] (2024)	32	62 ± 11.6	Systolic heart failure, refractory VA	Bilateral (27), unilateral (5)	1-year survival: 61.4%

2.4. Subcutaneous Nerve Stimulation

Subcutaneous nerve activity and superficial skin sympathetic nerve activity recorded in the chest wall correlate with SG activity [75–77]. This technique is likely originated from acupuncture. Stimulation at the Xinshu acupoint (BL15), located approximately 5 cm lateral to the spine at T5 level, has been shown to alter mRNA expression in sympathetic ganglia in a rat model [78]. Electrodes are positioned within the thoracic subcutaneous tissue near this region to deliver stimulation [78,79]. Preclinical work demonstrated the feasibility and efficacy of this novel technique to show a reduced sympathetic tone (3.5 mA, 10 Hz, 14 s ON and 1.1 min OFF) [78] and reduced fibrosis in persistent AF in a canine model (3.5 mA, 10 Hz, 20 s ON and 60 s OFF) [79]. Clinically, a prospective randomized trial to test whether chronic subcutaneous nerve stimulation can decrease AF burden was recently completed (STALL-AF [Using Electrical Nerve Stimulation to Control Atrial Fibrillation]; NCT04529941. The results of this study are not available yet and are expected to be released soon. In terms of VA, dogs with acute MI and increased risk of VT underwent subcutaneous nerve stimulation of the SG [80]. The outcomes showed decreased mean SG nerve activity after MI [80]. However, further clinical studies need to be performed to establish optimal stimulation protocols and long-term safety in humans.

3. Targeting the Spinal Cord and Dorsal Root Ganglion

3.1. Thoracic Epidural Anesthesia

Thoracic epidural anesthesia (TEA) is a common practice for relieving perioperative pain but has begun developing as a therapeutic method for arrhythmia treatment. The

sympathetic pathway from the spinal cord travels through the sympathetic chain, then to the heart; thus, the spinal cord is a prime target for interrupting sympathetic signals that may cause arrhythmia [81]. TEA has been shown to provide partial or selective sympathetic blockade by impeding spinal segments targeting the ventricles [16]. Therefore, TEA could inhibit fibers proximally to both the right and left SG, thereby reducing efferent output to the heart. TEA has been shown to increase the VF threshold during acute myocardial ischemia while also prolonging ventricular repolarization and the effective refractory period [82,83]. Additionally, TEA has been shown to suppress the effects of sympathoexcitation on the shortening of the ventricular activation recovery interval and the spatial heterogeneity of repolarization in the heart [84]. Applying local anesthetic epidurally causes almost immediate selective sympatholysis by reducing adrenergic output. The dose of TEA can be adjusted according to the patient's response [85]. The efficacy of this approach is influenced by factors such as dose concentration and catheter placement [86]. For instance, a study evaluating three different concentrations of ropivacaine TEA found that the highest concentration produced the most significant reduction in systemic vascular resistance [87]. Precise catheter insertion is critical, as incorrect placement has led to major complications in patients, including hematoma formation, nerve injury, local anesthetic systemic toxicity, ineffective analgesia, or unintended high/block spread [86].

In preclinical studies, TEA reduced the myocardial excitability induced by SG stimulation in pigs. It also showed TEA stabilizing the electrical wave, such as activation recovery interval, and markers of arrhythmogenesis, such as dispersion of repolarization [84]. The anti-arrhythmic effects of TEA are also attributed to increases in ventricular effective refractory periods, decreases in the slope of restitution, and decreases in the border zone heterogeneity [88]. One of the first clinical applications was reported in 2005, showing the effectiveness of TEA in reducing episodes of electrical storm [89]. Another case report appeared to show similar outcomes with TEA [90]. Both cases highlighted the usefulness of TEA to manage ventricular storms with little hemodynamic changes, even under other pharmacological agents being used. Do et al. reported a case series with patients who underwent TEA, showing a reduction of $\geq$80% in arrhythmia burden [85]. Another study showed that patients who had TEA followed by LSCD all survived to hospital discharge [63].

3.2. Spinal Cord Stimulation

Spinal cord stimulation (SCS) affects the cardiac nervous system centrally and peripherally [6,91]. SCS can intercept cardiac afferent signals from the heart and suppress efferent output from the intermediolateral region of the spinal cord within the spinal cord. This sympathetic efferent suppression leads to reduced cardiac sympathoexcitation back to the heart through the stellate ganglion, thus resulting in cardioprotective effects such as improvements in cardiac function and reduction in arrhythmias [14,92,93]. GABA-mediated pathways have been examined for SCS to work within the spinal cords in the pain field [94], but they still need further research in the cardiac field. SCS leads are typically situated in the epidural space percutaneously, and a programmable pulse generator (IPG) is implanted in the pocket in the back for delivering the stimulation. In terms of practical stimulation methods, no optimal stimulation method has been confirmed yet. SCS has shown effective pain relief in many clinical studies by applying traditional low-frequency stimulation at 50 Hz [95]; however, recently, kilohertz high-frequency stimulation has shown better pain relief in line with patients' satisfaction with less perception and less paresthesia [96,97]. For the purpose of arrhythmia treatment, there is even less known about the optimization of SCS. For example, how long the stimulation should be delivered is another question, and no optimal period has been determined yet. High-frequency stimulation

may represent a preferable approach, as it is associated with reduced paresthesia [98,99]. Kilohertz-frequency SCS has also been shown to produce longer-lasting inhibitory effects on myocardial ischemia-related spinal neurons compared to conventional low-frequency SCS [100]. Furthermore, computational modeling [101,102], combined with preclinical studies to validate these findings, could facilitate the identification of optimal stimulation parameters prior to clinical application.

Animal studies with SCS are showing promising effects in mitigating VAs and excitatory arrhythmogenesis. In pigs, low-frequency 50 Hz SCS targeting the T3/T4 spinal level was shown to reduce VTs and measures of cardiac electrophysiology and arrhythmogenesis, such as activation recovery interval and repolarization time shortening, dispersion of repolarization, and arrhythmia score [103]. The same research group posits that SCS reduces VAs by mitigating glial cell activation and activating GABA signaling pathways [104,105]. Another mechanism explored is the regulation of norepinephrine release; SCS significantly reduced norepinephrine levels associated with arrhythmogenesis in a canine cardiac ischemia model [106]. There is extensive preclinical research from physiological and mechanistic aspects to prevent VAs by SCS [105,107]; however, there are few clinical studies, possibly because of the invasive nature of the procedure and the use of anticoagulants in these cardiac patients. In the SCS HEART clinical study, SCS was shown to improve heart failure symptoms and to protect against VAs [92]. A study in 2015 showed that SCS minimized episodes of VT and fibrillation in a patient with severe electrical storm [108]. There are also several clinical studies focusing on the relief of angina pectoris with SCS [109,110].

In an AF canine model, SCS lengthens the atrial effective refractory period and decreases AF burden and inducibility [111]. When inducing atrial tachyarrhythmias and bradycardias in dogs, SCS obtunds the excitatory signals triggering arrhythmogenesis [112]. These effects are speculated to be modulated through decreased activity in the ICNS [113]. Autonomic remodeling of the right atrial GP and left SG caused by fast atrial pacing-induced AF was shown to be attenuated by SCS in the canine model [93]. In a recent clinical study, temporary SCS demonstrated efficacy for suppressing post-operative AF after coronary artery bypass grafting [114].

3.3. Dorsal Root Ganglion Stimulation

Cardio-spinal neural reflexes pass through the dorsal root ganglion (DRG) while traveling from primary afferent neurons to the dorsal horn at the thoracic level of the spinal cord [115]. As such, the DRG offers an accessible target for bioelectronic neuromodulation [116]. DRG stimulation (DRGS) electrodes can be placed in the prone position using fluoroscopic guidance, with the electrode positioned over the DRG in the dorsal region of the foramen [117]. There is evidence of DRGS relieving pain in preclinical studies [118–120], but there are few studies related to arrhythmia treatment. Currently, there are only animal studies for the application of DRGS in reducing arrhythmogenesis. In recent pig studies, thoracic DRGS decreased sympathoexcitation and ventricular arrhythmogenesis [121]. Also, it has been shown that thoracic DRGS reduced ventricular arrhythmogenesis using both low (20 Hz) and high (1 kHz) frequencies [122].

4. Targeting Parasympathetic Systems

4.1. Vagus Nerve Stimulation

The vagus nerve is the 10th cranial nerve, which contains both parasympathetic efferent and afferent axons in the nerve [123]. Based on these anatomical features, vagus nerve stimulation (VNS) can modulate the cardiac autonomic nervous system [6]. The VNS lead needs to be placed surgically in the neck, and the IPG is implanted in the chest for direct VNS [124]. Through this direct way of stimulation, both afferent and efferent axonal

paths are regulated [125,126]. Additionally, a noninvasive transcutaneous VNS approach at the tragus has been explored and has shown effectiveness in modulating cardiac autonomic imbalances [127–129]. There are no optimal stimulation parameters confirmed yet, but Ardell et al. mentioned a potential configuration to ensure the most effective delivery of invasive stimulation [91].

Many animal studies explore the effects of VNS on AF [130]. In one study, low-level VNS was shown to increase the threshold when trying to induce fibrillation with stimulation of other parts of the CANS, such as the GP, atrium, and pulmonary veins [131]. In canines, it is shown that VNS targets specific neuronal populations of the intrinsic cardiac system to attenuate the potential for AF [132].

There is controversy on whether VNS has antiarrhythmic effects or proarrhythmic effects. An early study had indicated that strong VNS (above 100% sensory thresholds) would induce AF, so moderate intensities (less than 80% of thresholds) can deliver therapeutic effects without risk of arrhythmia [133,134]. Additionally, distinct neurotransmitters have been shown to mediate different outcomes. The pro-arrhythmogenic effects of high-intensity VNS are driven by elevated levels of acetylcholine and vasoactive intestinal peptide, whereas the anti-arrhythmogenic effects observed at lower stimulation intensities are mediated by nitric oxide or phosphatidylinositol-3-kinase [134]. Clinical VNS applications normally use moderate intensities that cause mild-to-undetectable slowing of the heart rate [135] and can modulate heart rate variability depending on target location and stimulation parameters [136]. A more recent report by Stavrakis et al. showed that low-level VNS at a frequency of 20 Hz and 50% below the threshold for 72 h reduced the episodes of post-operative AF in patients undergoing cardiac surgery compared to the control group [137]. The same group also showed that transcutaneous VNS at a frequency of 20 Hz and 50% below the threshold for one hour decreased pacing-induced AF [138].

In terms of VAs, preclinical data support that VNS is effective in VA prevention [139,140]. Invasive VNS in canine models has shown a suppression of VA [139,141]. A recent study by Hu et al. has shown that MI rats treated with implantable remote-controlled VNS had significantly reduced incidence and duration of VAs after four weeks [142]. Additionally, noninvasive VNS of the tragus has also been shown to reduce arrhythmia inducibility in canines [143].

4.2. Baroreflex Activation Therapy

Baroreceptors are mechano-sensitive neurons in both the aortic arch and carotid sinus that modulate blood pressure and the autonomic nervous system [144]. Stimulating baroreceptors can stimulate afferent parasympathetic nerves, leading to an increase in parasympathetic tone and a decrease in sympathetic tone [145]. Stimulation of the carotid sinus is the common method for baroreceptor stimulation.

There is only preclinical evidence for baroreflex activation therapy to be effective in AAs [133]. In porcine models, carotid baroreceptor stimulation at levels commonly used for hypertension showed an increase in vagal tone, resulting in atrial effective refractory period shortening and increased AF inducibility [146]. On the contrary, in the canine model, reducing the magnitude of stimulation below the threshold to lower blood pressure decreased right atrial Ganglionated plexi (GP) neural activity and increased the atrial effective refractory period; thus, AF inducibility was reduced [147,148].

Similarly to AAs, there is a lack of clinical evidence for treating VAs, although a preclinical study showed a reduction in episodes of premature ventricular contractions during acute myocardial ischemia and VF [149].

4.3. Carotid Body Resection or Ablation

The carotid bodies (CBs) are bilaterally positioned at the bifurcation of the carotid arteries, strategically placed to ensure sufficient oxygen supply to the brain [150]. They are sensitive to small changes in blood oxygen, flow, carbon dioxide, and pH [151,152]. The CBs have strong reflex effects on the respiratory and cardiovascular systems [150,153]. This afferent system is normally inactive at resting conditions, but when hypoxia occurs, the CBs are triggered, increasing ventilation and sympathetic activity, while contributing to periodic breathing during sleep [154,155].

As it relates to arrhythmias, there are very few studies on CB ablation. However, in patients with heart failure, the overactivation of sympathetic tones is associated with chemoreflexes in the CBs [156]. Thus, the removal of these bodies can mitigate sympathetic activation. In a preclinical study, CB ablation was shown to reduce the number of AAs in rats with chronic hypoxia mimicking obstructive sleep apnea [157]. A study found that early CB ablation treatment in a rat model of chronic heart failure reduced ventricular arrhythmogenesis by eliminating the carotid chemoreflex drive associated with the heart failure state [158]. However, no clinical studies are exploring the therapeutic effects of CB ablation on cardiac arrhythmias.

5. Other Potential Neuromodulation Techniques

5.1. Renal Denervation

Renal sympathetic nerves contribute to cardiac function and sympathetic outflow to the kidneys [159]. Efferent sympathetic outflow triggers the release of renin, the increase in tubular sodium reabsorption, and the decrease in renal blood flow [160]. Many clinical trials have been performed to demonstrate the effectiveness of renal denervation to treat persistent hypertension by likely modulating sympathoexcitation in hypertension [17,161,162]. However, due to sympathetic nerves present in renal arteries and the role of sympathetic nerves in triggering arrhythmia, there is potential for renal denervation (RDN) to hinder arrhythmogenesis [163].

RDN led to a reduction in postinfarction VAs in pigs [164]. In canines, another study found similar results, concluding that RDN contributed to a reduction in neural remodeling in the heart and SG associated with MI, and thus, consequent arrhythmias [165]. VT can be a target for RDN, with one of the first clinical applications reported in 2012 [166]. Later, it was shown that adjunctive RDN was more effective than only VT ablation in the prevention of VT/VF without any procedure-related complications [167]. A more recent study by Bradfield et al. demonstrated the efficacy of radiofrequency-based RDN in treating refractory VT. Patients who underwent RDN as an adjunctive treatment to CSD had a reduction in ICD therapies when comparing 6 months pre-RDN versus 6 months post-RDN, with ICD shocks being a significant decrease [168].

Additionally, it has been shown that RDN can be effective in the treatment of AF [169]. RDN reduced the burden of AF at 12 months after the treatment [170]. Catheter ablation through the isolation of the pulmonary vein is an option for patients who have displeasing responses to pharmacological treatment for AF. Although more effective than drug treatment for minimizing AF recurrence [171], ablation has a 20% to 50% failure rate, resulting in repeat procedures [172,173]. Steinberg et al. investigated whether RDN, when combined with pulmonary vein isolation (PVI), could enhance long-term antiarrhythmic efficacy [174]. Among 283 patients, freedom from AF, tachycardia, or flutter after 12 months was observed in 56.5% of patients undergoing pulmonary vein isolation alone and in 72.1% of those undergoing PVI plus RDN [174].

5.2. Ganglionated Plexus Ablation

GP are autonomic ganglia on the epicardium, primarily within the epicardial fat [175]. Studies have shown that the GP consists of a heterogeneous neuronal population. This includes afferent, interconnecting, and efferent neurons, where interconnecting neurons account for most of the neural components in the GP [9]. Additionally, the GP acts as the communication center between the intrinsic and the extrinsic CANS, responsible for coordinating signal trafficking between afferent and efferent circuits [8]. In the body, the four major atrial GPs reside close to the pulmonary veins (PVs), and each innervates a respective PV and the nearby atrial myocardium [176,177]. The interconnections of the GP converge to the sinus node as well as the atrioventricular (AV) node via the anterior right GP and inferior right GP, respectively [178]. In humans, these neural pathways similarly connect the GP with the PVs, sinus node, and AV node [179].

GP ablation is performed either at their estimated anatomical locations or the location identified using high-frequency stimulation [180]. The best technique to perform GP ablation remains undecided.

In animal studies, there tend to be conflicting results on the arrhythmic effects of GP ablation. GP ablation was shown to be potentially proarrhythmic in canines [181]. Studies have shown that GP ablation increases the risk of VAs after myocardial ischemia [182], and GP ablation alone is not superior in maintaining AF-free survival [183]. A recent study demonstrated promising results, showing that targeted anatomical and high-frequency stimulation-guided epicardial pulsed field GP ablation prolongs the atrial effective refractory period and reduces both AF inducibility and duration [184].

Long-term effects of GP ablation have not been explored heavily, but a study posits that introducing other therapies along with GP ablation could help reduce the risks of arrhythmogenesis [185]. They showed that GP ablation and ligament of Marshall ablation mitigated paroxysmal arrhythmias [185]. Randomized clinical studies of the additional influence of GP ablation during PV isolation have been conflicting [186,187]. In a randomized study involving 242 patients undergoing PV isolation, Katritsis et al. found that those assigned to additional anatomically based GP ablation experienced a 47% relative reduction in the risk of recurrent atrial tachycardia or AF over a two-year follow-up period [188]. On the other hand, in the AF Ablation and Autonomic Modulation via Thoracoscopic Surgery (AFACT) study, GP ablation was performed thoracoscopically as an adjunct to PV isolation. Anatomical identification of GPs was guided by high-frequency stimulation to evoke vagal responses [187]. However, the study found that selective GP ablation without concomitant PVI did not significantly improve outcomes in patients with persistent AF [187]. These findings suggest that GP ablation alone may be insufficient as a standalone therapy for persistent AF but may have a synergistic effect when combined with PV isolation, potentially enhancing the efficacy of surgical ablation strategies.

Several factors may account for the conflicting outcomes observed with GP ablation, including variations in ablation techniques, differences in the AF subtypes targeted, and diverse underlying patient conditions [189,190]. Emerging technologies, such as advanced mapping systems, may help enhance the effectiveness of GP ablation [191,192].

5.3. Acupuncture

Acupuncture has a long history in the East, especially in China [193]. Acupuncture has been performed to treat cardiovascular diseases, spanning from hypertension to angina, and it is gaining popularity in the West [194]. There are numerous clinical studies suggesting the protective effect of acupuncture for cardiac ischemia and remodeling [195–199]. To perform acupuncture, needles are inserted into specific acupoints, each with its own specific targets and therapeutic effects [200]. In general, the effects of acupuncture appear more

pronounced when the patient has a sympathetic tone greater than normal at baseline [201]. Additionally, electroacupuncture has been explored by inducing electrical stimulation at the needle's target [202–204]. This methodology involves sending tolerable electrical stimulation through the needles at a desired frequency and intensity [204]. When it comes to cardiac arrhythmias, there are even fewer but promising studies for the application of acupuncture [205–207].

In rodents, multiple studies have shown that acupuncture reduces VAs. One study showed that targeting the PC6 pressure point with electroacupuncture reduced the arrhythmia score in rats during myocardial ischemia–reperfusion [206]. Zuo et al. similarly found that acupuncture attenuated the sympathetic tone by reducing the expression of inhibitors responsible for VAs [207]. Clinically, acupuncture has decreased the rate of AF recurrence in persistent AF patients [208]. The recurrence of AF can also be quantified as the AF burden, which accounts for the frequency of AF and how often the patient is in a state of AF [200]. Compared to control AF patients with a 54% recurrence rate, patients receiving acupuncture and amiodarone treatment had significantly lower recurrence rates of 35% and 27%, respectively [209]. Thus, acupuncture is approaching a similar therapeutic of medications.

5.4. Transcutaneous Magnetic Stimulation

Transcutaneous magnetic stimulation (TcMS) is a technique that takes advantage of the plasticity of a patient's nervous system and can contribute to excitation or inhibition depending on stimulation parameters [210,211]. This methodology is important not only due to its ability to change neural circuitry but also because it is noninvasive and nondestructive. TcMS is commonly used for treating pain and depression [212]. Also, it has been shown to impact heart rate variability and cardiac rhythm, causing minor parasympathetic activation [213]. However, TcMS can be targeted not only within the parasympathetic nervous system, such as the tragus, but also within the sympathetic nervous system, such as the SG [214].

TcMS of parasympathetic trunks was shown to suppress AF [214,215]. Preclinical evidence supports the promise of this non-invasive treatment to suppress AF, showing that in the canine model, the electromagnetic field stimulation reduced the burden of the AF caused by rapid atrial pacing [216]. Clinically, patients with paroxysmal AF were shown to have a reduced chance of AF and shorter episodes of pacing-induced AF using low-level electromagnetic fields [217]. In terms of the sympathetic nervous system, in a randomized trial of patients with VT storms who were treated with TcMS of the left SG, the burden of VAs decreased without adverse events [210,214]. Also, a more recent study showed a similar outcome with transcutaneous magnetic stimulation, with a reduction in episodes of VAs at 24 h post-treatment [20].

6. Conclusions

The neuromodulation of the CANS holds significant promise for the treatment of both atrial and ventricular arrhythmias. Among the available approaches, SGB and CSD currently have the most robust clinical evidence, particularly in the management of VAs. However, their invasive nature, variability in long-term efficacy, and the lack of large-scale randomized controlled trials present significant barriers to widespread adoption. Device-based therapies, such as VNS and SCS, are also promising; however, they face challenges including invasiveness, the need to establish optimal stimulation protocols, uncertainty regarding long-term efficacy, and a lack of large-scale randomized controlled trials. Future studies should prioritize the development of minimally invasive alternatives with comparable efficacy, while also addressing the critical need for rigorous randomized

clinical trials to evaluate long-term outcomes, durability of response, and patient selection strategies across different neuromodulatory approaches.

Author Contributions: Conceptualization, B.W., Y.K. and S.S.; investigation, B.W. and Y.K.; resources, S.S.; visualization, B.W.; writing—original draft preparation, B.W. and Y.K.; writing—review and editing, B.W., Y.K. and S.S.; supervision, S.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Not applicable.

Acknowledgments: The authors (B.W., Y.K. and S.S.) have reviewed and edited the output and take full responsibility for the content of this publication.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

CANS	Cardiac Autonomic Nervous System
SG	Stellate Ganglion
SGB	Stellate Ganglion Block
BoNT-A	Botulinum Toxin A
VA	Ventricular Arrhythmia
VF	Ventricular Fibrillation
AA	Atrial Arrhythmia
AF	Atrial Fibrillation
MI	Myocardial Infarction
CSD	Cardiac Sympathetic Denervation
QTc	Corrected QT
LCSD	Left Cardiac Sympathetic Denervation
BCSD	Bilateral Cardiac Sympathetic Denervation
ICD	Implantable Cardioverter-Defibrillator
VT	Ventricular Tachycardia
TEA	Thoracic Epidural Anesthesia
SCS	Spinal Cord Stimulation
IPG	Implantable Programmable Pulse Generator
DRG	Dorsal Root Ganglion
DRGS	Dorsal Root Ganglion Stimulation
VNS	Vagus Nerve Stimulation
GP	Ganglionated Plexi
CB	Carotid Body
RDN	Renal Denervation
PV	Pulmonary Vein
AV	Atrioventricular
AFACT	AF Ablation and Autonomic Modulation via Thoracoscopic Surgery
TcMS	Transcutaneous Magnetic Stimulation

References

1. Tang, D.H.; Gilligan, A.M.; Romero, K. Economic Burden and Disparities in Healthcare Resource Use Among Adult Patients with Cardiac Arrhythmia. *Appl. Health Econ. Health Policy* **2014**, *12*, 59–71. [CrossRef] [PubMed]
2. Sussman, M.; Menzin, J.; Lin, I.; Kwong, W.J.; Munsell, M.; Friedman, M.; Selim, M. Impact of atrial fibrillation on stroke-related healthcare costs. *J. Am. Heart Assoc.* **2013**, *2*, e000479. [CrossRef] [PubMed]
3. Chugh, S.S.; Reinier, K.; Teodorescu, C.; Evanado, A.; Kehr, E.; Al Samara, M.; Mariani, R.; Gunson, K.; Jui, J. Epidemiology of sudden cardiac death: Clinical and research implications. *Prog. Cardiovasc. Dis.* **2008**, *51*, 213–228. [CrossRef] [PubMed]

4. Ko, D.; Chung, M.K.; Evans, P.T.; Benjamin, E.J.; Helm, R. Atrial Fibrillation: A Review. *JAMA* **2025**, *333*, 329–342. [CrossRef] [PubMed]
5. Samuel, M.; Healey, J.S.; Nault, I.; Sterns, L.D.; Essebag, V.; Gray, C.; Hruczkowski, T.; Gardner, M.; Parkash, R.; Sapp, J.L. Ventricular Tachycardia and ICD Therapy Burden With Catheter Ablation Versus Escalated Antiarrhythmic Drug Therapy. *JACC Clin. Electrophysiol.* **2023**, *9*, 808–821. [CrossRef] [PubMed]
6. Herring, N.; Kalla, M.; Paterson, D.J. The autonomic nervous system and cardiac arrhythmias: Current concepts and emerging therapies. *Nat. Rev. Cardiol.* **2019**, *16*, 707–726. [CrossRef] [PubMed]
7. Fukuda, K.; Kanazawa, H.; Aizawa, Y.; Ardell, J.L.; Shivkumar, K. Cardiac innervation and sudden cardiac death. *Circ. Res.* **2015**, *116*, 2005–2019. [CrossRef] [PubMed]
8. Giannino, G.; Braia, V.; Brookles, C.G.; Giacobbe, F.; D'ascenzo, F.; Angelini, F.; Saglietto, A.; De Ferrari, G.M.; Dusi, V. The Intrinsic Cardiac Nervous System: From Pathophysiology to Therapeutic Implications. *Biology* **2024**, *13*, 105. [CrossRef] [PubMed]
9. Shivkumar, K.; Ardell, J.L. Cardiac autonomic control in health and disease. *J. Physiol.* **2016**, *594*, 3851. [CrossRef] [PubMed]
10. Ajijola, O.A.; Aksu, T.; Arora, R.; Biaggioni, I.; Chen, P.; De Ferrari, G.; Dusi, V.; Fudim, M.; Goldberger, J.J.; Green, A.L.; et al. Clinical neurocardiology: Defining the value of neuroscience-based cardiovascular therapeutics—2024 update. *J. Physiol.* **2025**, *603*, 1781–1839. [CrossRef] [PubMed]
11. Shen, M.J.; Zipes, D.P. Role of the autonomic nervous system in modulating cardiac arrhythmias. *Circ. Res.* **2014**, *114*, 1004–1021. [CrossRef] [PubMed]
12. Salavatian, S.; Beaumont, E.; Gibbons, D.; Hammer, M.; Hoover, D.B.; Armour, J.A.; Ardell, J.L. Thoracic spinal cord and cervical vagosympathetic neuromodulation obtund nodose sensory transduction of myocardial ischemia. *Auton. Neurosci.* **2017**, *208*, 57–65. [CrossRef] [PubMed]
13. Salavatian, S.; Ardell, S.M.; Hammer, M.; Gibbons, D.; Armour, J.A.; Ardell, J.L. Thoracic spinal cord neuromodulation obtunds dorsal root ganglion afferent neuronal transduction of the ischemic ventricle. *Am. J. Physiol. Heart Circ. Physiol.* **2019**, *317*, H1134–H1141. [CrossRef] [PubMed]
14. Salavatian, S.; Kuwabara, Y.; Wong, B.; Fritz, J.R.; Howard-Quijano, K.; Foreman, R.D.; Armour, J.A.; Ardell, J.L.; Mahajan, A. Spinal neuromodulation mitigates myocardial ischemia-induced sympathoexcitation by suppressing the intermediolateral nucleus hyperactivity and spinal neural synchrony. *Front. Neurosci.* **2023**, *17*, 1180294. [CrossRef] [PubMed]
15. Ichikawa, Y.; Matsumoto, S.; Fujinaka, W.; Takatori, M.; Nishioka, K.; Namera, A. Left Stellate Ganglion Blockade for Refractory Ventricular Arrhythmias With Aconitine Poisoning: A Case Report. *A A Pract.* **2023**, *17*, e01666. [CrossRef] [PubMed]
16. Wink, J.; Veering, B.T.; Aarts, L.P.H.J.; Wouters, P.F. Effects of Thoracic Epidural Anesthesia on Neuronal Cardiac Regulation and Cardiac Function. *Anesthesiology* **2019**, *130*, 472–491. [CrossRef] [PubMed]
17. Mahfoud, F.; E Kandzari, D.; Kario, K.; Townsend, R.R.; A Weber, M.; E Schmieder, R.; Tsioufis, K.; Pocock, S.; Dimitriadis, K.; Choi, J.W.; et al. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): A randomised, sham-controlled trial. *Lancet* **2022**, *399*, 1401–1410. [CrossRef] [PubMed]
18. Bradfield, J.S.; Ajijola, O.A.; Vaseghi, M.; Shivkumar, K. Mechanisms and management of refractory ventricular arrhythmias in the age of autonomic modulation. *Heart Rhythm* **2018**, *15*, 1252–1260. [CrossRef] [PubMed]
19. Lemery, R. Cardiac Neuromodulation and Neurocardiology. *J. Cardiovasc. Electrophysiol.* **2025**, *36*, 863–873. [CrossRef] [PubMed]
20. Markman, T.M.; Gugger, D.; Arkles, J.; Riley, M.P.; Dixit, S.; Guandalini, G.S.; Frankel, D.S.; Epstein, A.E.; Callans, D.J.; Singhal, S.; et al. Neuromodulation for the Treatment of Refractory Ventricular Arrhythmias. *JACC Clin. Electrophysiol.* **2023**, *9*, 161–169. [CrossRef] [PubMed]
21. Consoli, L.N.; Cetinel, E.; Lajczak, P.; Koziakas, I.G.; Majeed, M.W.; Wijaya, P.; Salha, I.; Samanidis, G. Surgical neuromodulation therapies to prevent postoperative atrial fibrillation: A meta-analysis, meta-regression, and trial sequential analysis of randomized controlled trials. *Heart Rhythm*, 2025; *in press*. [CrossRef] [PubMed]
22. Cha, Y.; Li, X.; Yang, M.; Han, J.; Wu, G.; Kapa, S.C.; McLeod, C.J.; Noseworthy, P.A.; Mulpuru, S.K.; Asirvatham, S.J.; et al. Stellate ganglion block and cardiac sympathetic denervation in patients with inappropriate sinus tachycardia. *J. Cardiovasc. Electrophysiol.* **2019**, *30*, 2920–2928. [CrossRef] [PubMed]
23. Ganesh, A.; Qadri, Y.J.; Boortz-Marx, R.L.; Al-Khatib, S.M.; Harpole, D.H.; Katz, J.N.; Koontz, J.I.; Mathew, J.P.; Ray, N.D.; Sun, A.Y.; et al. Stellate Ganglion Blockade: An Intervention for the Management of Ventricular Arrhythmias. *Curr. Hypertens. Rep.* **2020**, *22*, 100. [CrossRef] [PubMed]
24. Dusi, V.; Angelini, F.; Gravinese, C.; Frea, S.; De Ferrari, G.M. The role of antiarrhythmic drugs and stellate ganglion block in the acute management of electrical storm. *Eur. Heart J. Suppl.* **2025**, *27* (Suppl. S1), i154–i161. [CrossRef] [PubMed]
25. Yeo, Y.H.; Thong, J.Y.; Tan, M.-C.; Lee, J.Z.; Tan, J.L.; Markman, T.; Rattanawong, P. Stellate ganglion block for refractory ventricular arrhythmias: An updated systematic review. *J. Interv. Card. Electrophysiol.* **2025**, *68*, 427–431. [CrossRef] [PubMed]
26. Savastano, S.; Baldi, E.; Compagnoni, S.; Rordorf, R.; Sanzo, A.; Gentile, F.R.; Dusi, V.; Frea, S.; Gravinese, C.; Cauti, F.M.; et al. Electrical storm treatment by percutaneous stellate ganglion block: The STAR study. *Eur. Heart J.* **2024**, *45*, 823–833. [CrossRef] [PubMed]

27. Chouairi, F.; Rajkumar, K.; Benak, A.; Qadri, Y.; Piccini, J.P.; Mathew, J.; Ray, N.D.; Toman, J.; Kautzner, J.; Ganesh, A.; et al. A Multicenter Study of Stellate Ganglion Block as a Temporizing Treatment for Refractory Ventricular Arrhythmias. *JACC Clin. Electrophysiol.* **2024**, *10*, 750–758. [CrossRef] [PubMed]
28. Zhang, S.; Wang, M.; Jiao, L.; Liu, C.; Chen, H.; Zhou, L.; Wang, Y.; Wang, Y.; Liu, Z.; Liu, Z.; et al. Ultrasound-guided injection of botulinum toxin type A blocks cardiac sympathetic ganglion to improve cardiac remodeling in a large animal model of chronic myocardial infarction. *Heart Rhythm* **2022**, *19*, 2095–2104. [CrossRef] [PubMed]
29. Reinertsen, E.; Sabayon, M.; Riso, M.; Lloyd, M.; Spektor, B. Stellate ganglion blockade for treating refractory electrical storm: A historical cohort study. *Can. J. Anaesth.* **2021**, *68*, 1683–1689. [CrossRef] [PubMed]
30. Sanghai, S.; Abbott, N.J.; Dewland, T.A.; Henrikson, C.A.; Elman, M.R.; Wollenberg, M.; Ivie, R.; Gonzalez-Sotomayor, J.; Nazer, B. Stellate Ganglion Blockade With Continuous Infusion Versus Single Injection for Treatment of Ventricular Arrhythmia Storm. *JACC Clin. Electrophysiol.* **2021**, *7*, 452–460. [CrossRef] [PubMed]
31. Pak, A.T.; Üstün, I.; Sengul, Y. Botulinum toxin type A wear-off phenomenon in chronic migraine patients: How long does the maximum efficiency last? *Arq. Neuropsiquiatr.* **2021**, *79*, 886–890. [CrossRef] [PubMed]
32. Kamanli, A.; Kaya, A.; Ardicoglu, O.; Ozgocmen, S.; Zengin, F.O.; Bayık, Y. Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. *Rheumatol. Int.* **2005**, *25*, 604–611. [CrossRef] [PubMed]
33. Lai, Z.-H.; Zheng, L.-H.; Yao, Y. Ultrasound-guided stellate ganglion blockade: An appealing tactic for cardiac electrical storm. *J. Geriatr. Cardiol.* **2023**, *20*, 376–382. [CrossRef] [PubMed]
34. Bhattaram, S.; Shinde, V.; Hm, A. Star in the storm: Percutaneous stellate ganglion blockade for drug-refractory electrical storm in the emergency department. *Clin. Exp. Emerg. Med.* **2023**, *10*, 122–124. [CrossRef] [PubMed]
35. Wittwer, E.D.; Radosevich, M.A.; Ritter, M.; Cha, Y.-M. Stellate Ganglion Blockade for Refractory Ventricular Arrhythmias: Implications of Ultrasound-Guided Technique and Review of the Evidence. *J. Cardiothorac. Vasc. Anesth.* **2020**, *34*, 2245–2252. [CrossRef] [PubMed]
36. Savastano, S.; Dusi, V.; Baldi, E.; Rordorf, R.; Sanzo, A.; Camporotondo, R.; Fracchia, R.; Compagnoni, S.; Frigerio, L.; Visconti, L.O.; et al. Anatomical-based percutaneous left stellate ganglion block in patients with drug-refractory electrical storm and structural heart disease: A single-centre case series. *Europace* **2021**, *23*, 581–586. [CrossRef] [PubMed]
37. Motazedian, P.; Quinn, N.; Wells, G.A.; Beauregard, N.; Lam, E.; Mathieu, M.-E.; Knoll, W.; Prosperi-Porta, G.; Ly, V.; Parlow, S.; et al. Efficacy of stellate ganglion block in treatment of electrical storm: A systematic review and meta-analysis. *Sci. Rep.* **2024**, *14*, 24719. [CrossRef] [PubMed]
38. Gulcu-Bulut, N.; Gonca, E.; Kocoglu, H.; Bozdoğan, Ö.; Karaaslan, K. Pretreatment with stellate ganglion blockade before ischemia reduces infarct size in rat hearts. *Saudi Med. J.* **2010**, *31*, 148–152. [PubMed]
39. Gu, Y.; Wang, L.; Wang, X.; Tang, Y.; Cao, F.; Fang, Y. Assessment of ventricular electrophysiological characteristics at periinfarct zone of postmyocardial infarction in rabbits following stellate ganglion block. *J. Cardiovasc. Electrophysiol.* **2012**, *23* (Suppl. S1), S29–S35. [CrossRef] [PubMed]
40. Callipari, C.; Stone, M.; John, D.; Keceli, M.; Giles, R.A. Intra-Cardiac Arrest Use of Stellate Ganglion Block for Refractory Ventricular Tachycardia. *J. Emerg. Med.* **2023**, *64*, 628–634. [CrossRef] [PubMed]
41. Fudim, M.; Qadri, Y.J.; Waldron, N.H.; Boortz-Marx, R.L.; Ganesh, A.; Patel, C.B.; Podgoreanu, M.V.; Sun, A.Y.; Milano, C.A.; Tong, B.C.; et al. Stellate Ganglion Blockade for the Treatment of Refractory Ventricular Arrhythmias. *JACC Clin. Electrophysiol.* **2020**, *6*, 562–571. [CrossRef] [PubMed]
42. Yang, X.; Zhang, L.; Liu, H.; Shao, Y.; Zhang, S. Cardiac Sympathetic Denervation Suppresses Atrial Fibrillation and Blood Pressure in a Chronic Intermittent Hypoxia Rat Model of Obstructive Sleep Apnea. *J. Am. Heart Assoc.* **2019**, *8*, e010254. [CrossRef] [PubMed]
43. Meng, L.; Tseng, C.H.; Shivkumar, K.; Ajijola, O. Efficacy of Stellate Ganglion Blockade in Managing Electrical Storm: A Systematic Review. *JACC Clin. Electrophysiol.* **2017**, *3*, 942–949. [CrossRef] [PubMed]
44. Baldi, E.; Dusi, V.; Rordorf, R.; Currao, A.; Compagnoni, S.; Sanzo, A.; Gentile, F.R.; Frea, S.; Gravinese, C.; Angelini, F.; et al. Efficacy of early use of percutaneous stellate ganglion block for electrical storms. *Eur. Heart J. Acute Cardiovasc. Care* **2024**, *13*, 757–765. [CrossRef] [PubMed]
45. Yang, F.; Du, Y.; Yuan, C.; Han, L.; Zhao, Y.; Xie, Y.; Peng, W. Effect of ultrasound-guided stellate ganglion block on cerebral oxygen metabolism and S100B protein during carotid endarterectomy. *Am. J. Transl. Res.* **2024**, *16*, 1018. [CrossRef] [PubMed]
46. Leftheriotis, D.; Flevari, P.; Kossyvakis, C.; Katsaras, D.; Batistaki, C.; Arvaniti, C.; Giannopoulos, G.; Deftereos, S.; Kostopanagiotou, G.; Lekakis, J. Acute effects of unilateral temporary stellate ganglion block on human atrial electrophysiological properties and atrial fibrillation inducibility. *Heart Rhythm* **2016**, *13*, 2111–2117. [CrossRef] [PubMed]
47. Groenendyk, J.; Mandler, A.; Luan, D.; Goljo, E.; Tedore, T.; Cheung, J.W.; Markowitz, S.M. Management of Rapid Atrial Fibrillation Using Stellate Ganglion Blockade. *JACC Case Rep.* **2024**, *29*, 102530. [CrossRef] [PubMed]
48. Rao, B.H.; Lokre, A.; Patnala, N.; Padmanabhan, T.N.C. Stellate ganglion ablation by conventional radiofrequency in patients with electrical storm. *Europace* **2023**, *25*, euad290. [CrossRef] [PubMed]

49. Liu, S.; Yu, X.; Luo, D.; Qin, Z.; Wang, X.; He, W.; Ma, R.; Hu, H.; Xie, J.; He, B.; et al. Ablation of the Ligament of Marshall and Left Stellate Ganglion Similarly Reduces Ventricular Arrhythmias During Acute Myocardial Infarction. *Circ. Arrhythm. Electrophysiol.* **2018**, *11*, e005945. [CrossRef] [PubMed]
50. Wang, Y.; He, S.; Xiong, X.; Liu, J.; Xie, B.; Yao, Y.; Yin, J.; Zi, L.; Wang, X.; Tang, Y.; et al. Left Stellate Ganglion Ablation Inhibits Ventricular Arrhythmias through Macrophage Regulation in Canines with Acute Ischemic Stroke. *Int. J. Med. Sci.* **2021**, *18*, 891–901. [CrossRef] [PubMed]
51. Shelton, R.S.; Ogawa, M.; Lin, H.; Shen, C.; Wong, J.; Lin, S.-F.; Chen, P.-S.; Everett, T.H. Effects of Stellate Ganglion Cryoablation on Subcutaneous Nerve Activity and Atrial Tachyarrhythmias in a Canine Model of Pacing-Induced Heart Failure. *JACC Clin. Electrophysiol.* **2018**, *4*, 686–695. [CrossRef] [PubMed]
52. Shah, A.J.; Wittbrodt, M.T.; Bremner, J.D.; Vaccarino, V. Cardiovascular pathophysiology from the cardioneural perspective and its clinical applications. *Trends Cardiovasc. Med.* **2022**, *32*, 172–177. [CrossRef] [PubMed]
53. Buckley, U.; Yamakawa, K.; Takamiya, T.; Armour, J.A.; Shivkumar, K.; Ardell, J.L. Targeted stellate decentralization: Implications for sympathetic control of ventricular electrophysiology. *Heart Rhythm.* **2016**, *13*, 282–288. [CrossRef] [PubMed]
54. Irie, T.; Yamakawa, K.; Hamon, D.; Nakamura, K.; Shivkumar, K.; Vaseghi, M. Cardiac sympathetic innervation via middle cervical and stellate ganglia and antiarrhythmic mechanism of bilateral stellectomy. *Am. J. Physiol.-Heart Circ. Physiol.* **2017**, *312*, H392–H405. [CrossRef] [PubMed]
55. Dhanse, S.; Rao, M.S.; Ramachandran, P.; Devasia, T.; Ashwal, A.J.; Paramasivam, G.; Prabhu, M. Effectiveness of ultrasonography-guided cardiac sympathetic denervation in acute control of electrical storm: A retrospective case series. *J. Anaesthesiol. Clin. Pharmacol.* **2022**, *38*, 610–616. [CrossRef] [PubMed]
56. Melinosky, K.; Leng, A.; Johnson, C.R.; Verdi, K.G.; Etchill, E.W.; Tandri, H.; Brock, M.V.; Ha, J.S. Outcomes Comparison of Robot-Assisted and Video-Assisted Thoracoscopic Cardiac Sympathetic Denervation. *Innovations* **2023**, *18*, 512–518. [CrossRef] [PubMed]
57. Dusi, V.; Sorg, J.M.; Gornbein, J.; Gima, J.; Yanagawa, J.; Lee, J.M.; Vecerek, N.; Vaseghi, M.; Bradfield, J.S.; De Ferrari, G.M.; et al. Prognostic impact of atrial rhythm and dimension in patients with structural heart disease undergoing cardiac sympathetic denervation for ventricular arrhythmias. *Heart Rhythm* **2020**, *17 Pt A*, 714–720. [CrossRef] [PubMed]
58. Moss, A.J.; McDonald, J. Unilateral cervicothoracic sympathetic ganglionectomy for the treatment of long QT interval syndrome. *New Engl. J. Med.* **1971**, *285*, 903–904. [CrossRef] [PubMed]
59. Schwartz, P.J.; Snebold, N.G.; Brown, A.M. Effects of unilateral cardiac sympathetic denervation on the ventricular fibrillation threshold. *Am. J. Cardiol.* **1976**, *37*, 1034–1040. [CrossRef] [PubMed]
60. Schwartz, P.J.; Priori, S.G.; Cerrone, M.; Spazzolini, C.; Odero, A.; Napolitano, C.; Bloise, R.; De Ferrari, G.M.; Klersy, C.; Moss, A.J.; et al. Left cardiac sympathetic denervation in the management of high-risk patients affected by the long-QT syndrome. *Circulation* **2004**, *109*, 1826–1833. [CrossRef] [PubMed]
61. Surman, T.L.; Stuklis, R.G.; Chan, J.C. Thoracoscopic Sympathectomy for Long QT Syndrome. Literature Review and Case Study. *Heart Lung Circ.* **2019**, *28*, 486–494. [CrossRef] [PubMed]
62. Ertugrul, I.; Donmez, Y.N.; Aydın, A.; Aykan, H.H.; Sel, K.; Uysal, S.; Yilmaz, M.; Karagoz, T. Bilateral thoracoscopic sympathectomy for cardiac denervation in pediatric population: Does Kuntz nerve cauterization have an impact on success? *J. Card. Surg.* **2021**, *36*, 2705–2713. [CrossRef] [PubMed]
63. Bourke, T.; Vaseghi, M.; Michowitz, Y.; Sankhla, V.; Shah, M.; Swapna, N.; Boyle, N.G.; Mahajan, A.; Narasimhan, C.; Lokhandwala, Y.; et al. Neuraxial modulation for refractory ventricular arrhythmias: Value of thoracic epidural anesthesia and surgical left cardiac sympathetic denervation. *Circulation* **2010**, *121*, 2255–2262. [CrossRef] [PubMed]
64. Hanna, D.B.; Karimianpour, A.; Mamprejew, N.; Fiechter, C.; Verghese, D.; Navas, V.; Sharma, D. The role of cardiac sympathetic denervation for ventricular arrhythmias: An updated systematic review and meta-analysis. *J. Interv. Card. Electrophysiol.* **2025**, *68*, 415–425. [CrossRef] [PubMed]
65. Assis, F.R.; Sharma, A.; Shah, R.; Akhtar, T.; Adari, S.; Calkins, H.; Ha, J.S.; Mandal, K.; Tandri, H. Long-Term Outcomes of Bilateral Cardiac Sympathetic Denervation for Refractory Ventricular Tachycardia. *JACC Clin. Electrophysiol.* **2021**, *7*, 463–470. [CrossRef] [PubMed]
66. Ahmed, A.; Charate, R.; Bawa, D.; Ghazal, R.; Garg, J.; Pothineni, N.V.K.; Kabra, R.; Della Rocca, D.G.; Atkins, D.; Lakkireddy, P.; et al. Bilateral Cardiac Sympathetic Denervation for Refractory Multifocal Premature Ventricular Contractions in Patients With Nonischemic Cardiomyopathy. *JACC Clin. Electrophysiol.* **2024**, *10*, 31–39. [CrossRef] [PubMed]
67. Vaseghi, M.; Barwad, P.; Corrales, F.J.M.; Tandri, H.; Mathuria, N.; Shah, R.; Sorg, J.M.; Gima, J.; Mandal, K.; Morales, L.C.S.; et al. Cardiac Sympathetic Denervation for Refractory Ventricular Arrhythmias. *J. Am. Coll. Cardiol.* **2017**, *69*, 3070–3080. [CrossRef] [PubMed]
68. Hofferberth, S.C.; Cecchin, F.; Loberman, D.; Fynn-Thompson, F. Left thoracoscopic sympathectomy for cardiac denervation in patients with life-threatening ventricular arrhythmias. *J. Thorac. Cardiovasc. Surg.* **2014**, *147*, 404–409. [CrossRef] [PubMed]

69. Cai, C.; Dai, M.; Tian, Y.; Zhang, P.; Wittwer, E.D.; Rho, R.H.; Kapa, S.; McLeod, C.J.; Mulpuru, S.K.; Lee, H.; et al. Electrophysiologic effects and outcomes of sympatholysis in patients with recurrent ventricular arrhythmia and structural heart disease. *J. Cardiovasc. Electrophysiol.* **2019**, *30*, 1499–1507. [CrossRef] [PubMed]
70. Shah, R.; Assis, F.; Alugubelli, N.; Okada, D.R.; Cardoso, R.; Shivkumar, K.; Tandri, H. Cardiac sympathetic denervation for refractory ventricular arrhythmias in patients with structural heart disease: A systematic review. *Heart Rhythm* **2019**, *16*, 1499–1505. [CrossRef] [PubMed]
71. Barwad, P.; Sinkar, K.; Bachani, N.; Shah, R.; Shah, V.; Kumar, B.; Bhoskar, S.; Desai, N.; Lokhandwala, Y. Long-term clinical outcomes of cardiac sympathetic denervation in patients with refractory ventricular arrhythmias. *J. Cardiovasc. Electrophysiol.* **2021**, *32*, 1065–1074. [CrossRef] [PubMed]
72. Yalin, K.; Liosis, S.; Palade, E.; Fink, T.; Schierholz, S.; Sawan, N.; Eitel, C.; Heeger, C.H.; Sciacca, V.; Sano, M.; et al. Cardiac sympathetic denervation in patients with nonischemic cardiomyopathy and refractory ventricular arrhythmias: A single-center experience. *Clin. Res. Cardiol.* **2021**, *110*, 21–28. [CrossRef] [PubMed]
73. König, S.; Schröter, T.; A Borger, M.; Bertagnolli, L.; Nedios, S.; Darma, A.; Hindricks, G.; Arya, A.; Dinov, B. Outcomes following cardiac sympathetic denervation in patients with structural heart disease and refractory ventricular arrhythmia. *Europace* **2022**, *24*, 1800–1808. [CrossRef] [PubMed]
74. Brady, S.; Matthia, E.; Antoine, S.; Aranda, J.; Miles, W.; Vilaro, J.; Al-Ani, M.; Oduntan, O.; Guo, Y.; Li, Y.; et al. Outcome of Patients With Systolic Heart Failure Who Underwent Sympathectomy for Ventricular Arrhythmia. *Am. J. Cardiol.* **2024**, *225*, 37–40. [CrossRef] [PubMed]
75. Robinson, E.A.; Rhee, K.; Doytchinova, A.; Kumar, M.; Shelton, R.; Jiang, Z.; Kamp, N.J.; Adams, D.; Wagner, D.; Shen, C.; et al. Estimating sympathetic tone by recording subcutaneous nerve activity in ambulatory dogs. *J. Cardiovasc. Electrophysiol.* **2015**, *26*, 70–78. [CrossRef] [PubMed]
76. Doytchinova, A.; Patel, J.; Zhou, S.; Chen, L.S.; Lin, H.; Shen, C.; Everett, T.H.; Lin, S.-F.; Chen, P.-S. Subcutaneous nerve activity and spontaneous ventricular arrhythmias in ambulatory dogs. *Heart Rhythm* **2015**, *12*, 612–620. [CrossRef] [PubMed]
77. Jiang, Z.; Zhao, Y.; Doytchinova, A.; Kamp, N.J.; Tsai, W.-C.; Yuan, Y.; Adams, D.; Wagner, D.; Shen, C.; Chen, L.S.; et al. Using skin sympathetic nerve activity to estimate stellate ganglion nerve activity in dogs. *Heart Rhythm* **2015**, *12*, 1324–1332. [CrossRef] [PubMed]
78. Yuan, Y.; Jiang, Z.; Zhao, Y.; Tsai, W.-C.; Patel, J.; Chen, L.S.; Shen, C.; Lin, S.-F.; Chen, H.-S.V.; Everett, T.H.; et al. Long-term intermittent high-amplitude subcutaneous nerve stimulation reduces sympathetic tone in ambulatory dogs. *Heart Rhythm* **2018**, *15*, 451–459. [CrossRef] [PubMed]
79. Kusayama, T.; Wan, J.; Yuan, Y.; Liu, X.; Li, X.; Shen, C.; Fishbein, M.C.; Everett, T.H.; Chen, P.-S. Effects of subcutaneous nerve stimulation with blindly inserted electrodes on ventricular rate control in a canine model of persistent atrial fibrillation. *Heart Rhythm* **2021**, *18*, 261–270. [CrossRef] [PubMed]
80. Yuan, Y.; Zhao, Y.; Wong, J.; Tsai, W.-C.; Jiang, Z.; Kabir, R.A.; Han, S.; Shen, C.; Fishbein, M.C.; Chen, L.S.; et al. Subcutaneous nerve stimulation reduces sympathetic nerve activity in ambulatory dogs with myocardial infarction. *Heart Rhythm* **2020**, *17*, 1167–1175. [CrossRef] [PubMed]
81. Boezaart, A.P.; Smith, C.R.; Chembrovich, S.; Zasimovich, Y.; Server, A.; Morgan, G.; Theron, A.; Booysen, K.; A Reina, M. Visceral versus somatic pain: An educational review of anatomy and clinical implications. *Reg. Anesth. Pain. Med.* **2021**, *46*, 629–636. [CrossRef] [PubMed]
82. Hoang, J.D.; van Weperen, V.Y.; Kang, K.-W.; Jani, N.R.; Swid, M.A.; Chan, C.A.; Lokhandwala, Z.A.; Lux, R.L.; Vaseghi, M. Antiarrhythmic Mechanisms of Epidural Blockade After Myocardial Infarction. *Circ. Res.* **2024**, *135*, e57–e75. [CrossRef] [PubMed]
83. Kang, K.W. Successful neural modulation of bedside modified thoracic epidural anesthesia for ventricular tachycardia electrical storm. *Acute Crit. Care* **2022**, *39*, 643–646. [CrossRef] [PubMed]
84. Howard-Quijano, K.; Takamiya, T.; Dale, E.A.; Yamakawa, K.; Zhou, W.; Buckley, U.; Mahajan, A. Effect of Thoracic Epidural Anesthesia on Ventricular Excitability in a Porcine Model. *Anesthesiology* **2017**, *126*, 1096–1106. [CrossRef] [PubMed]
85. Do, D.H.; Bradfield, J.; Ajijola, O.A.; Vaseghi, M.; Le, J.; Rahman, S.; Mahajan, A.; Nogami, A.; Boyle, N.G.; Shivkumar, K. Thoracic Epidural Anesthesia Can Be Effective for the Short-Term Management of Ventricular Tachycardia Storm. *J. Am. Heart Assoc.* **2017**, *6*, e007080. [CrossRef] [PubMed]
86. Kumar, K.; Horner, F.; Aly, M.; Nair, G.S.; Lin, C. Why do thoracic epidurals fail? A literature review on thoracic epidural failure and catheter confirmation. *World J. Crit. Care Med.* **2024**, *13*, 94157. [CrossRef] [PubMed]
87. Hong, J.-M.; Lee, H.J.; Oh, Y.-J.; Cho, A.R.; Kim, H.J.; Lee, D.-W.; Do, W.-S.; Kwon, J.-Y.; Kim, H. Observations on significant hemodynamic changes caused by a high concentration of epidurally administered ropivacaine: Correlation and prediction study of stroke volume variation and central venous pressure in thoracic epidural anesthesia. *BMC Anesthesiol.* **2017**, *17*, 153. [CrossRef] [PubMed]

88. Hoang, J.D.; van Weperen, V.Y.; Kang, K.W.; Jani, N.R.; Swid, M.A.; Chan, C.A.; Lokhandwala, Z.A.; Lux, R.L.; Vaseghi, M. Thoracic epidural blockade after myocardial infarction benefits from anti-arrhythmic pathways mediated in part by parasympathetic modulation. *bioRxiv* **2024**. bioRxiv:2024.03.14.585127.
89. Smith, D.I.; Kralovic, S.A.; Hegazy, R.A.; Tran, H. Continuous Thoracic Paravertebral Block to Treat Electrical Storm. *Tex. Heart Inst. J.* **2022**, *49*, e176433. [CrossRef] [PubMed]
90. Shinde, S.R.; Basantwani, S.; Tendolkar, B. Management of ventricular storm with thoracic epidural anesthesia. *Ann. Card. Anaesth.* **2019**, *22*, 439–441. [CrossRef] [PubMed]
91. Ardell, J.L.; Nier, H.; Hammer, M.; Southerland, E.M.; Ardell, C.L.; Beaumont, E.; KenKnight, B.H.; Armour, J.A. Defining the neural fulcrum for chronic vagus nerve stimulation: Implications for integrated cardiac control. *J. Physiol.* **2017**, *595*, 6887–6903. [CrossRef] [PubMed]
92. Liao, S.-Y.; Liu, Y.; Zuo, M.; Zhang, Y.; Yue, W.; Au, K.-W.; Lai, W.-H.; Wu, Y.; Shuto, C.; Chen, P.; et al. Remodelling of cardiac sympathetic re-innervation with thoracic spinal cord stimulation improves left ventricular function in a porcine model of heart failure. *Europace* **2015**, *17*, 1875–1883. [CrossRef] [PubMed]
93. Wang, S.; Zhou, X.; Huang, B.; Wang, Z.; Zhou, L.; Chen, M.; Yu, L.; Jiang, H. Spinal cord stimulation suppresses atrial fibrillation by inhibiting autonomic remodeling. *Heart Rhythm* **2016**, *13*, 274–281. [CrossRef] [PubMed]
94. Caylor, J.; Reddy, R.; Yin, S.; Cui, C.; Huang, M.; Huang, C.; Rao, R.; Baker, D.G.; Simmons, A.; Souza, D.; et al. Spinal cord stimulation in chronic pain: Evidence and theory for mechanisms of action. *Bioelectron. Med.* **2019**, *5*, 12. [CrossRef] [PubMed]
95. Sdrulla, A.D.; Guan, Y.; Raja, S.N. Spinal Cord Stimulation: Clinical Efficacy and Potential Mechanisms. *Pain. Pract.* **2018**, *18*, 1048–1067. [CrossRef] [PubMed]
96. Kapural, L.; Yu, C.; Doust, M.W.; Gliner, B.E.; Vallejo, R.; Sitzman, B.T.; Amirdelfan, K.; Morgan, D.M.; Brown, L.L.; Yearwood, T.L.; et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain. *Anesthesiology* **2015**, *123*, 851–860. [CrossRef] [PubMed]
97. Conic, R.R.Z.; Caylor, J.; Cui, C.L.; Reyes, Z.; Nelson, E.; Yin, S.; Lerman, I. Sex-specific differences in the efficacy of traditional low frequency versus high frequency spinal cord stimulation for chronic pain. *Bioelectron. Med.* **2022**, *8*, 8. [CrossRef] [PubMed]
98. Hoelzer, B.C.; Edgar, D.; Lu, S.-P.; Taylor, R.S. Indirect Comparison of 10 kHz Spinal Cord Stimulation (SCS) versus Traditional Low-Frequency SCS for the Treatment of Painful Diabetic Neuropathy: A Systematic Review of Randomized Controlled Trials. *Biomedicines* **2022**, *10*, 2630. [CrossRef] [PubMed]
99. Sagalajev, B.; Zhang, T.; Abdollahi, N.; Yousefpour, N.; Medlock, L.; Al-Basha, D.; Ribeiro-Da-Silva, A.; Esteller, R.; Ratté, S.; Prescott, S.A. Absence of paresthesia during high-rate spinal cord stimulation reveals importance of synchrony for sensations evoked by electrical stimulation. *Neuron* **2024**, *112*, 404–420.e6. [CrossRef] [PubMed]
100. Salavatian, S.; Wong, B.; Kuwabara, Y.; Fritz, J.R.; Varghese, C.G.; Howard-Quijano, K.; Armour, J.A.; Foreman, R.D.; Ardell, J.L.; Mahajan, A. Comparing the Memory Effects of 50-Hz Low-Frequency and 10-kHz High-Frequency Thoracic Spinal Cord Stimulation on Spinal Neural Network in a Myocardial Infarction Porcine Model. *Neuromodulation* **2024**, *27*, 1177–1186. [CrossRef] [PubMed]
101. Solanes, C.; Durá, J.L.; Canós, M.Á.; De Andrés, J.; Martí-Bonmatí, L.; Saiz, J. 3D patient-specific spinal cord computational model for SCS management: Potential clinical applications. *J. Neural Eng.* **2021**, *18*, 036017. [CrossRef] [PubMed]
102. Rogers, E.R.; Mirzakhalili, E.; Lempka, S.F. Model-based analysis of subthreshold mechanisms of spinal cord stimulation for pain. *J. Neural Eng.* **2023**, *20*, 066003. [CrossRef] [PubMed]
103. Howard-Quijano, K.; Takamiya, T.; Dale, E.A.; Kipke, J.; Kubo, Y.; Grogan, T.; Afyouni, A.; Shivkumar, K.; Mahajan, A. Spinal cord stimulation reduces ventricular arrhythmias during acute ischemia by attenuation of regional myocardial excitability. *Am. J. Physiol. Heart Circ. Physiol.* **2017**, *313*, H421–H431. [CrossRef] [PubMed]
104. Howard-Quijano, K.; Yamaguchi, T.; Gao, F.; Kuwabara, Y.; Puig, S.; Lundquist, E.; Salavatian, S.; Taylor, B.; Mahajan, A. Spinal Cord Stimulation Reduces Ventricular Arrhythmias by Attenuating Reactive Gliosis and Activation of Spinal Interneurons. *JACC Clin. Electrophysiol.* **2021**, *7*, 1211–1225. [CrossRef] [PubMed]
105. Howard-Quijano, K.; Kuwabara, Y.; Yamaguchi, T.; Roman, K.; Salavatian, S.; Taylor, B.; Mahajan, A. GABAergic signaling during spinal cord stimulation reduces cardiac arrhythmias in a porcine model. *Anesthesiology* **2023**, *138*, 372–387. [CrossRef] [PubMed]
106. Ardell, J.L.; Foreman, R.D.; Armour, J.A.; Shivkumar, K. Cardiac sympathectomy and spinal cord stimulation attenuate reflex-mediated norepinephrine release during ischemia preventing ventricular fibrillation. *JCI Insight* **2019**, *4*, 131648. [CrossRef] [PubMed]
107. Wang, S.; Zhou, X.; Huang, B.; Wang, Z.; Liao, K.; Saren, G.; Lu, Z.; Chen, M.; Yu, L.; Jiang, H. Spinal cord stimulation protects against ventricular arrhythmias by suppressing left stellate ganglion neural activity in an acute myocardial infarction canine model. *Heart Rhythm* **2015**, *12*, 1628–1635. [CrossRef] [PubMed]
108. Walega, D.; Rosenow, J.M. Spinal cord stimulation for electrical storm refractory to conventional medical treatment: An emerging indication? *Neuromodulation Technol. Neural Interface* **2015**, *18*, 194–196. [CrossRef] [PubMed]

109. Saraste, A.; Ukkonen, H.; Varis, A.; Vasankari, T.; Tunturi, S.; Taittonen, M.; Rautakorpi, P.; Luotolahti, M.; Airaksinen, K.J.; Knuuti, J. Effect of spinal cord stimulation on myocardial perfusion reserve in patients with refractory angina pectoris. *Eur. Heart J. Cardiovasc. Imaging* **2015**, *16*, 449–455. [CrossRef] [PubMed]
110. Pan, X.; Bao, H.; Si, Y.; Xu, C.; Chen, H.; Gao, X.; Xie, X.; Xu, Y.; Sun, F.; Zeng, L. Spinal Cord Stimulation for Refractory Angina Pectoris: A Systematic Review and Meta-analysis. *Clin. J. Pain.* **2017**, *33*, 543–551. [CrossRef] [PubMed]
111. Bernstein, S.A.; Wong, B.; Vasquez, C.; Rosenberg, S.P.; Rooke, R.; Kuznekoff, L.M.; Lader, J.M.; Mahoney, V.M.; Budylin, T.; Älvstrand, M.; et al. Spinal cord stimulation protects against atrial fibrillation induced by tachypacing. *Heart Rhythm* **2012**, *9*, 1426–1433.e3. [CrossRef] [PubMed]
112. Li, P.; Chang, Y.; Song, J. Advances in preclinical surgical therapy of cardiovascular diseases. *Int. J. Surg.* **2024**, *110*, 4965–4975. [CrossRef] [PubMed]
113. Yu, L.; Huang, B.; He, W.; Wang, S.; Liao, K.; Zhou, X.; He, B.; Lu, Z.; Jiang, H. Spinal cord stimulation suppresses focal rapid firing–induced atrial fibrillation by inhibiting atrial ganglionated plexus activity. *J. Cardiovasc. Pharmacol.* **2014**, *64*, 554–559. [CrossRef] [PubMed]
114. Romanov, A.; Lomivorotov, V.; Chernyavskiy, A.; Murtazin, V.; Kliver, E.; Ponomarev, D.; Mikheenko, I.; Yakovlev, A.; Yakovleva, M.; Steinberg, J.S. Temporary spinal cord stimulation to prevent postcardiac surgery atrial fibrillation: 30-day safety and efficacy outcomes. *J. Am. Coll. Cardiol.* **2022**, *79*, 754–756. [CrossRef] [PubMed]
115. Ardell, J.L.; Andresen, M.C.; Armour, J.A.; Billman, G.E.; Chen, P.-S.; Foreman, R.D.; Herring, N.; O'Leary, D.S.; Sabbah, H.N.; Schultz, H.; et al. Translational neurocardiology: Preclinical models and cardioneural integrative aspects. *J. Physiol.* **2016**, *594*, 3877–3909. [CrossRef] [PubMed]
116. Krames, E.S. The dorsal root ganglion in chronic pain and as a target for neuromodulation: A review. *Neuromodulation Technol. Neural Interface* **2015**, *18*, 24–32. [CrossRef] [PubMed]
117. Sverrisdottir, Y.B.; Martin, S.C.; Hadjipavlou, G.; Kent, A.R.; Paterson, D.J.; FitzGerald, J.J.; Green, A.L. Human Dorsal Root Ganglion Stimulation Reduces Sympathetic Outflow and Long-Term Blood Pressure. *JACC Basic. Transl. Sci.* **2020**, *5*, 973–985. [CrossRef] [PubMed]
118. Deer, T.R.; Levy, R.M.; Kramer, J.; Poree, L.; Amirdelfan, K.; Grigsby, E.; Staats, P.; Burton, A.W.; Burgher, A.H.; Obray, J.; et al. Dorsal root ganglion stimulation yielded higher treatment success rate for CRPS and causalgia at 3 and 12 months: Randomized comparative trial. *Pain* **2017**, *158*, 669–681. [CrossRef] [PubMed]
119. Deer, T.R.; Hunter, C.W.; Mehta, P.; Sayed, D.; Grider, J.S.; Lamer, T.J.; E Pope, J.; Falowski, S.; A Provenzano, D.; Esposito, M.F.; et al. A systematic literature review of dorsal root ganglion neurostimulation for the treatment of pain. *Pain Med.* **2020**, *21*, 1581–1589. [CrossRef] [PubMed]
120. D'sOuza, R.S.; Kubrova, E.; Her, Y.F.; Barman, R.A.; Smith, B.J.; Alvarez, G.M.; West, T.E.; Abd-Elsayed, A. Dorsal root ganglion stimulation for lower extremity neuropathic pain syndromes: An evidence-based literature review. *Adv. Ther.* **2022**, *39*, 4440–4473. [CrossRef] [PubMed]
121. Kuwabara, Y.; Howard-Quijano, K.; Salavatian, S.; Yamaguchi, T.; Saba, S.; Mahajan, A. Thoracic dorsal root ganglion stimulation reduces acute myocardial ischemia induced ventricular arrhythmias. *Front. Neurosci.* **2023**, *17*, 1091230. [CrossRef] [PubMed]
122. Kuwabara, Y.; Salavatian, S.; Howard-Quijano, K.; Yamaguchi, T.; Lundquist, E.; Mahajan, A. Neuromodulation With Thoracic Dorsal Root Ganglion Stimulation Reduces Ventricular Arrhythmogenicity. *Front. Physiol.* **2021**, *12*, 713717. [CrossRef] [PubMed]
123. Garamendi-Ruiz, I.; Gomez-Esteban, J.C. Cardiovascular autonomic effects of vagus nerve stimulation. *Clin. Auton. Res.* **2019**, *29*, 183–194. [CrossRef] [PubMed]
124. De Ferrari, G.M.; Crijns, H.J.; Borggrefe, M.; Milasinovic, G.; Smid, J.; Zabel, M.; Gavazzi, A.; Sanzo, A.; Dennert, R.; Kuschyk, J.; et al. Chronic vagus nerve stimulation: A new and promising therapeutic approach for chronic heart failure. *Eur. Heart J.* **2011**, *32*, 847–855. [CrossRef] [PubMed]
125. Ardell, J.L.; Rajendran, P.S.; Nier, H.A.; KenKnight, B.H.; Armour, J.A. Central-peripheral neural network interactions evoked by vagus nerve stimulation: Functional consequences on control of cardiac function. *Am. J. Physiol. Heart Circ. Physiol.* **2015**, *309*, H1740–H1752. [CrossRef] [PubMed]
126. Yoo, P.B.; Liu, H.; Hincapie, J.G.; Ruble, S.B.; Hamann, J.J.; Grill, W.M. Modulation of heart rate by temporally patterned vagus nerve stimulation in the anesthetized dog. *Physiol. Rep.* **2016**, *4*, e12689. [CrossRef] [PubMed]
127. Stavrakis, S.; Stoner, J.A.; Humphrey, M.B.; Morris, L.; Filiberti, A.; Reynolds, J.C.; Elkholey, K.; Javed, I.; Twidale, N.; Riha, P.; et al. TREAT AF (Transcutaneous Electrical Vagus Nerve Stimulation to Suppress Atrial Fibrillation): A Randomized Clinical Trial. *JACC Clin. Electrophysiol.* **2020**, *6*, 282–291. [CrossRef] [PubMed]
128. Antonino, D.; Teixeira, A.L.; Maia-Lopes, P.M.; Souza, M.C.; Sabino-Carvalho, J.L.; Murray, A.R.; Deuchars, J.; Vianna, L.C. Non-invasive vagus nerve stimulation acutely improves spontaneous cardiac baroreflex sensitivity in healthy young men: A randomized placebo-controlled trial. *Brain Stimul.* **2017**, *10*, 875–881. [CrossRef] [PubMed]

129. Katsunuma, R.; Takamura, T.; Yamada, M.; Sekiguchi, A. Proof of mechanism investigation of Transcutaneous auricular vagus nerve stimulation through simultaneous measurement of autonomic functions: A randomized controlled trial protocol. *Biopsychosoc. Med.* **2024**, *18*, 15. [CrossRef] [PubMed]
130. Sheng, X.; Scherlag, B.J.; Yu, L.; Li, S.; Ali, R.; Zhang, Y.; Fu, G.; Nakagawa, H.; Jackman, W.M.; Lazzara, R.; et al. Prevention and reversal of atrial fibrillation inducibility and autonomic remodeling by low-level vagosympathetic nerve stimulation. *J. Am. Coll. Cardiol.* **2011**, *57*, 563–571. [CrossRef] [PubMed]
131. Yu, L.; Scherlag, B.J.; Li, S.; Sheng, X.; Lu, Z.; Nakagawa, H.; Zhang, Y.; Jackman, W.M.; Lazzara, R.; Jiang, H.; et al. Low-level vagosympathetic nerve stimulation inhibits atrial fibrillation inducibility: Direct evidence by neural recordings from intrinsic cardiac ganglia. *J. Cardiovasc. Electrophysiol.* **2011**, *22*, 455–463. [CrossRef] [PubMed]
132. Salavatian, S.; Beaumont, E.; Longpré, J.-P.; Armour, J.A.; Vinet, A.; Jacquemet, V.; Shivkumar, K.; Ardell, J.L. Vagal stimulation targets select populations of intrinsic cardiac neurons to control neurally induced atrial fibrillation. *Am. J. Physiol. Heart Circ. Physiol.* **2016**, *311*, H1311–H1320. [CrossRef] [PubMed]
133. Hanna, P.; Buch, E.; Stavrakis, S.; Meyer, C.; Tompkins, J.D.; Ardell, J.L.; Shivkumar, K. Neuroscientific therapies for atrial fibrillation. *Cardiovasc. Res.* **2021**, *117*, 1732–1745. [CrossRef] [PubMed]
134. Kharbanda, R.K.; van der Does, W.F.; van Staveren, L.N.; Taverne, Y.J.; Bogers, A.J.; de Groot, N.M. Vagus Nerve Stimulation and Atrial Fibrillation: Revealing the Paradox. *Neuromodulation Technol. Neural Interface* **2022**, *25*, 356–365. [CrossRef] [PubMed]
135. Zhang, Y.; Mazgalev, T.N. Arrhythmias and vagus nerve stimulation. *Heart Fail. Rev.* **2011**, *16*, 147–161. [CrossRef] [PubMed]
136. Machetanz, K.; Berelidze, L.; Guggenberger, R.; Gharabaghi, A. Transcutaneous auricular vagus nerve stimulation and heart rate variability: Analysis of parameters and targets. *Auton. Neurosci.* **2021**, *236*, 102894. [CrossRef] [PubMed]
137. Stavrakis, S.; Humphrey, M.B.; Scherlag, B.; Iftikhar, O.; Parwani, P.; Abbas, M.; Filiberti, A.; Fleming, C.; Hu, Y.; Garabelli, P.; et al. Low-Level Vagus Nerve Stimulation Suppresses Post-Operative Atrial Fibrillation and Inflammation: A Randomized Study. *JACC Clin. Electrophysiol.* **2017**, *3*, 929–938. [CrossRef] [PubMed]
138. Stavrakis, S.; Humphrey, M.B.; Scherlag, B.J.; Hu, Y.; Jackman, W.M.; Nakagawa, H.; Lockwood, D.; Lazzara, R.; Po, S.S. Low-level transcutaneous electrical vagus nerve stimulation suppresses atrial fibrillation. *J. Am. Coll. Cardiol.* **2015**, *65*, 867–875. [CrossRef] [PubMed]
139. Nasi-Er, B.; Wenhui, Z.; HuaXin, S.; Xianhui, Z.; Yaodong, L.; Yanmei, L.; Hongli, W.; TuEr-Hong, Z.; Qina, Z.; BaoPeng, T. Vagus nerve stimulation reduces ventricular arrhythmias and increases ventricular electrical stability. *Pacing Clin. Electrophysiol.* **2019**, *42*, 247–256. [CrossRef] [PubMed]
140. Stavrakis, S.; Kulkarni, K.; Singh, J.P.; Katritsis, D.G.; Armoundas, A.A. Autonomic Modulation of Cardiac Arrhythmias: Methods to Assess Treatment and Outcomes. *JACC Clin. Electrophysiol.* **2020**, *6*, 467–483. [CrossRef] [PubMed]
141. Zhang, L.; Lu, Y.; Sun, J.; Zhou, X.; Tang, B. Subthreshold vagal stimulation suppresses ventricular arrhythmia and inflammatory response in a canine model of acute cardiac ischaemia and reperfusion. *Exp. Physiol.* **2016**, *101*, 41–49. [CrossRef] [PubMed]
142. Hu, F.; Wang, Y.; Zang, M.; Li, G.; Wang, G.; Hu, D.; Zheng, L.; Yao, Y.; Pu, J. Remote-controlled vagal nerve stimulation attenuates ventricular arrhythmias and prevents heart failure progression in a rat model of acute myocardial infarction. *Auton. Neurosci.* **2025**, *260*, 103279. [CrossRef] [PubMed]
143. Yu, L.; Wang, S.; Zhou, X.; Wang, Z.; Huang, B.; Liao, K.; Saren, G.; Chen, M.; Po, S.S.; Jiang, H. Chronic Intermittent Low-Level Stimulation of Tragus Reduces Cardiac Autonomic Remodeling and Ventricular Arrhythmia Inducibility in a Post-Infarction Canine Model. *JACC Clin. Electrophysiol.* **2016**, *2*, 330–339. [CrossRef] [PubMed]
144. Armstrong, M.; Kerndt, C.C.; Moore, R.A. Physiology, Baroreceptors. In *StatPearls*; StatPearls Publishing: Treasure Island, FL, USA, 2024.
145. Abraham, W.T.; Zile, M.R.; Weaver, F.A.; Butter, C.; Ducharme, A.; Halbach, M.; Klug, D.; Lovett, E.G.; Müller-Ehmsen, J.; Schafer, J.E.; et al. Baroreflex Activation Therapy for the Treatment of Heart Failure With a Reduced Ejection Fraction. *JACC Heart Fail.* **2015**, *3*, 487–496. [CrossRef] [PubMed]
146. Linz, D.; Mahfoud, F.; Schotten, U.; Ukena, C.; Neuberger, H.; Wirth, K.; Böhm, M. Effects of electrical stimulation of carotid baroreflex and renal denervation on atrial electrophysiology. *J. Cardiovasc. Electrophysiol.* **2013**, *24*, 1028–1033. [CrossRef] [PubMed]
147. Liao, K.; Yu, L.; Zhou, X.; Saren, G.; Wang, S.; Wang, Z.; Huang, B.; Yang, K.; Jiang, H. Low-level baroreceptor stimulation suppresses atrial fibrillation by inhibiting ganglionated plexus activity. *Can. J. Cardiol.* **2015**, *31*, 767–774. [CrossRef] [PubMed]
148. Dai, M.; Bao, M.; Zhang, Y.; Yu, L.; Cao, Q.; Tang, Y.; Huang, H.; Wang, X.; Hu, D.; Huang, C. Low-level carotid baroreflex stimulation suppresses atrial fibrillation by inhibiting left stellate ganglion activity in an acute canine model. *Heart Rhythm* **2016**, *13*, 2203–2212. [CrossRef] [PubMed]
149. Liao, K.; Yu, L.; Yang, K.; Saren, G.; Wang, S.; Huang, B.; Jiang, H.; Resstel, L.B.M. Low-level carotid baroreceptor stimulation suppresses ventricular arrhythmias during acute ischemia. *PLoS ONE* **2014**, *9*, e109313. [CrossRef] [PubMed]
150. Iturriaga, R.; Alcayaga, J.; Chapleau, M.W.; Somers, V.K. Carotid body chemoreceptors: Physiology, pathology, and implications for health and disease. *Physiol. Rev.* **2021**, *101*, 1177–1235. [CrossRef] [PubMed]

151. Ding, Y.; Li, Y.; Schultz, H.D. Role of blood flow in carotid body chemoreflex function in heart failure. *J. Physiol.* **2011**, *589*, 245–258. [CrossRef] [PubMed]
152. Prabhakhar, N.R.; Joyner, M.J. Tasting arterial blood: What do the carotid chemoreceptors sense? *Front. Physiol.* **2015**, *5*, 524. [CrossRef] [PubMed]
153. Kumar, P. Systemic effects resulting from carotid body stimulation–invited article. *Arter. Chemorecept.* **2009**, 223–233. [CrossRef]
154. Whayne, T.F., Jr. Cardiovascular medicine at high altitude. *Angiology* **2014**, *65*, 459–472. [CrossRef] [PubMed]
155. Bilo, G.; Villafuerte, F.C.; Faini, A.; Anza-Ramírez, C.; Revera, M.; Giuliano, A.; Caravita, S.; Gregorini, F.; Lombardi, C.; Salvioni, E.; et al. Ambulatory Blood Pressure in Untreated and Treated Hypertensive Patients at High Altitude: The High Altitude Cardiovascular Research–Andes Study. *Hypertension* **2015**, *65*, 1266–1272. [CrossRef] [PubMed]
156. Marcus, N.J.; Del Rio, R.; Schultz, H.D. Central role of carotid body chemoreceptors in disordered breathing and cardiorenal dysfunction in chronic heart failure. *Front. Physiol.* **2014**, *5*, 438. [CrossRef] [PubMed]
157. Del Rio, R.; Andrade, D.C.; Lucero, C.; Arias, P.; Iturriaga, R. Carotid Body Ablation Abrogates Hypertension and Autonomic Alterations Induced by Intermittent Hypoxia in Rats. *Hypertension* **2016**, *68*, 436–445. [CrossRef] [PubMed]
158. Del Rio, R.; Marcus, N.J.; Schultz, H.D. Carotid chemoreceptor ablation improves survival in heart failure: Rescuing autonomic control of cardiorespiratory function. *J. Am. Coll. Cardiol.* **2013**, *62*, 2422–2430. [CrossRef] [PubMed]
159. Zheng, H.; Patel, K.P. Integration of renal sensory afferents at the level of the paraventricular nucleus dictating sympathetic outflow. *Auton. Neurosci.* **2017**, *204*, 57–64. [CrossRef] [PubMed]
160. Sata, Y.; Head, G.A.; Denton, K.; May, C.N.; Schlaich, M.P. Role of the Sympathetic Nervous System and Its Modulation in Renal Hypertension. *Front. Med.* **2018**, *5*, 82. [CrossRef] [PubMed]
161. Kario, K.; Yokoi, Y.; Okamura, K.; Fujihara, M.; Ogoyama, Y.; Yamamoto, E.; Urata, H.; Cho, J.-M.; Kim, C.-J.; Choi, S.-H.; et al. Catheter-based ultrasound renal denervation in patients with resistant hypertension: The randomized, controlled REQUIRE trial. *Hypertens. Res.* **2022**, *45*, 221–231. [CrossRef] [PubMed]
162. Mahfoud, F.; Weber, M.; Schmieder, R.E.; Lobo, M.D.; Blankestijn, P.J.; Persu, A.; Fischell, T.A.; Parise, H.; Pathak, A.; Kandzari, D.E. Catheter-based alcohol-mediated renal denervation for the treatment of uncontrolled hypertension: Design of two sham-controlled, randomized, blinded trials in the absence (TARGET BP OFF-MED) and presence (TARGET BP I) of antihypertensive medications. *Am. Heart J.* **2021**, *239*, 90–99. [CrossRef] [PubMed]
163. Goyal, A.; Jain, H.; Verma, A.; Jain, J.; Shamim, U.; Kanagala, S.G.; Motwani, J.; Dey, R.C.; Chunawala, Z.; Sohail, A.H.; et al. The role of renal denervation in cardiology and beyond: An updated comprehensive review and future directives. *Curr. Probl. Cardiol.* **2024**, *49*, 102196. [CrossRef] [PubMed]
164. Jackson, N.; Gizurarson, S.; Azam, M.A.; King, B.; Ramadeen, A.; Zamiri, N.; Porta-Sánchez, A.; Al-Hesayen, A.; Graham, J.; Kusha, M.; et al. Effects of Renal Artery Denervation on Ventricular Arrhythmias in a Postinfarct Model. *Circ. Cardiovasc. Interv.* **2017**, *10*, e004172. [CrossRef] [PubMed]
165. Zhang, W.; Zhou, Q.; Lu, Y.; Li, Y.; Zhang, L.; Zhang, J.; Xing, Q.; Lv, W.; Cheng, X.; Zhang, G.; et al. Renal Denervation Reduced Ventricular Arrhythmia After Myocardial Infarction by Inhibiting Sympathetic Activity and Remodeling. *J. Am. Heart Assoc.* **2018**, *7*, e009938. [CrossRef] [PubMed]
166. Ukena, C.; Bauer, A.; Mahfoud, F.; Schreieck, J.; Neuberger, H.-R.; Eick, C.; Sobotka, P.A.; Gawaz, M.; Böhm, M. Renal sympathetic denervation for treatment of electrical storm: First-in-man experience. *Clin. Res. Cardiol.* **2012**, *101*, 63–67. [CrossRef] [PubMed]
167. Evranos, B.; Canpolat, U.; Kocyigit, D.; Coteli, C.; Yorgun, H.; Aytemir, K. Role of adjuvant renal sympathetic denervation in the treatment of ventricular arrhythmias. *Am. J. Cardiol.* **2016**, *118*, 1207–1210. [CrossRef] [PubMed]
168. Bradfield, J.S.; Hayase, J.; Liu, K.; Moriarty, J.; Kee, S.T.; Do, D.; Ajijola, O.A.; Vaseghi, M.; Gima, J.; Sorg, J.; et al. Renal denervation as adjunctive therapy to cardiac sympathetic denervation for ablation refractory ventricular tachycardia. *Heart Rhythm* **2020**, *17*, 220–227. [CrossRef] [PubMed]
169. Nammas, W.; Airaksinen, J.K.; Paana, T.; Karjalainen, P.P. Renal sympathetic denervation for treatment of patients with atrial fibrillation: Reappraisal of the available evidence. *Heart Rhythm* **2016**, *13*, 2388–2394. [CrossRef] [PubMed]
170. Feyz, L.; Theuns, D.A.; Bhagwandien, R.; Strachinaru, M.; Kardys, I.; Van Mieghem, N.M.; Daemen, J. Atrial fibrillation reduction by renal sympathetic denervation: 12 months' results of the AFFORD study. *Clin. Res. Cardiol.* **2019**, *108*, 634–642. [CrossRef] [PubMed]
171. Mark, D.B.; Anstrom, K.J.; Sheng, S.; Piccini, J.P.; Baloch, K.N.; Monahan, K.H.; Daniels, M.R.; Bahnson, T.D.; Poole, J.E.; Rosenberg, Y.; et al. Effect of catheter ablation vs. medical therapy on quality of life among patients with atrial fibrillation: The CABANA randomized clinical trial. *JAMA* **2019**, *321*, 1275–1285. [CrossRef] [PubMed]
172. Calkins, H.; Hindricks, G.; Cappato, R.; Kim, Y.H.; Saad, E.B.; Aguinaga, L.; Akar, J.G.; Badhwar, V.; Brugada, J.; Camm, J.; et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Ep Europace* **2018**, *20*, e1–e160. [CrossRef] [PubMed]

173. Packer, D.L.; Mark, D.B.; Robb, R.A.; Monahan, K.H.; Bahnson, T.D.; Poole, J.E.; Noseworthy, P.A.; Rosenberg, Y.D.; Jeffries, N.; Mitchell, L.B.; et al. Effect of catheter ablation vs. antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: The CABANA randomized clinical trial. *JAMA* **2019**, *321*, 1261–1274. [CrossRef] [PubMed]
174. Steinberg, J.S.; Shabanov, V.; Ponomarev, D.; Losik, D.; Ivanickiy, E.; Kropotkin, E.; Polyakov, K.; Ptaszynski, P.; Keweloh, B.; Yao, C.J.; et al. Effect of Renal Denervation and Catheter Ablation vs. Catheter Ablation Alone on Atrial Fibrillation Recurrence Among Patients With Paroxysmal Atrial Fibrillation and Hypertension: The ERADICATE-AF Randomized Clinical Trial. *JAMA* **2020**, *323*, 248–255. [CrossRef] [PubMed]
175. Stavrakis, S.; Po, S. Ganglionated plexi ablation: Physiology and clinical applications. *Arrhythmia Electrophysiol. Rev.* **2017**, *6*, 186. [CrossRef] [PubMed]
176. Aksu, T.; Yalin, K.; Bozyel, S.; Gopinathannair, R.; Gupta, D. The anatomical basis behind the neuromodulation effects associated with pulmonary vein isolation. *J. Cardiovasc. Electrophysiol.* **2021**, *32*, 1733–1736. [CrossRef] [PubMed]
177. Saburkina, I.; Pauziene, N.; Solomon, O.I.; Rysevaite-Kyguoliene, K.; Pauza, D.H. Comparative gross anatomy of epicardiac ganglionated nerve plexi on the human and sheep cardiac ventricles. *Anat. Rec.* **2023**, *306*, 2302–2312. [CrossRef] [PubMed]
178. Zhang, M.; Wang, X.; Xie, X.; Wang, Z.; Liu, X.; Guan, J.; Wang, W.; Li, Z.; Wang, J.; Gao, M.; et al. Long-Term Effects of Atrial Ganglionated Plexi Ablation on Function and Structure of Sinoatrial and Atrioventricular Node in Canine. *Pacing Clin. Electrophysiol.* **2015**, *38*, 1181–1191. [CrossRef] [PubMed]
179. Malcolme-Lawes, L.C.; Lim, P.B.; Wright, I.; Kojodjojo, P.; Koa-Wing, M.; Jamil-Copley, S.; Dehbi, H.-M.; Francis, D.P.; Davies, D.W.; Peters, N.S.; et al. Characterization of the left atrial neural network and its impact on autonomic modification procedures. *Circ. Arrhythmia Electrophysiol.* **2013**, *6*, 632–640. [CrossRef] [PubMed]
180. Guo, Y.; Li, Y.; Li, S.; Ma, J.; Liu, J.; Ruan, Y.; Zhang, J. Comparative study of the therapeutic effects of radiofrequency ablation of ganglionated plexi guided by high-frequency stimulation and anatomical localization methods in the treatment of vagal syncope in young people. *Cardiology* **2024**, 418–426. [CrossRef] [PubMed]
181. Mao, J.; Yin, X.; Zhang, Y.; Yan, Q.; Dong, J.; Ma, C.; Liu, X. Ablation of epicardial ganglionated plexi increases atrial vulnerability to arrhythmias in dogs. *Circ. Arrhythm. Electrophysiol.* **2014**, *7*, 711–717. [CrossRef] [PubMed]
182. He, B.; Lu, Z.; He, W.; Wu, L.; Cui, B.; Hu, X.; Yu, L.; Huang, C.; Jiang, H. Effects of ganglionated plexi ablation on ventricular electrophysiological properties in normal hearts and after acute myocardial ischemia. *Int. J. Cardiol.* **2013**, *168*, 86–93. [CrossRef] [PubMed]
183. Choi, E.-K.; Chen, P.-S. Is the Atrial Neural Plexis a Therapeutic Target in Atrial Fibrillation? *Methodist. Debakey Cardiovasc. J.* **2015**, *11*, 82–86. [CrossRef] [PubMed]
184. Hertel, J.N.; Nissen, S.D.; Lindberg, L.A.; Schneider, M.; Niskala, A.; Isaksen, J.L.; Jerltorp, K.; Ye, C.; Hermans, B.J.M.; Aerts, L.; et al. Targeted epicardial pulsed field ablation of atrial ganglionated plexi: Electrophysiological and histological analysis in pigs. *Heart Rhythm*, 2025; *in press*. [CrossRef] [PubMed]
185. Zhao, Y.; Jiang, Z.; Tsai, W.-C.; Yuan, Y.; Chinda, K.; Choi, E.-K.; Fishbein, M.C.; Lin, S.-F.; Chen, P.-S.; Everett, T.H. Ganglionated plexi and ligament of Marshall ablation reduces atrial vulnerability and causes stellate ganglion remodeling in ambulatory dogs. *Heart Rhythm* **2016**, *13*, 2083–2090. [CrossRef] [PubMed]
186. Berger, W.R.; Neefs, J.; van den Berg, N.W.; Krul, S.P.; van Praag, E.M.; Piersma, F.R.; de Jong, J.S.S.G.; van Boven, W.-J.P.; Driessen, A.H.G.; de Groot, J.R. Additional Ganglion Plexus Ablation During Thoracoscopic Surgical Ablation of Advanced Atrial Fibrillation: Intermediate Follow-Up of the AFACT Study. *JACC Clin. Electrophysiol.* **2019**, *5*, 343–353. [CrossRef] [PubMed]
187. Kampaktsis, P.N.; Oikonomou, E.K.; Choi, D.Y.; Cheung, J.W. Efficacy of ganglionated plexi ablation in addition to pulmonary vein isolation for paroxysmal versus persistent atrial fibrillation: A meta-analysis of randomized controlled clinical trials. *J. Interv. Card. Electrophysiol.* **2017**, *50*, 253–260. [CrossRef] [PubMed]
188. Katritsis, D.G.; Pokushalov, E.; Romanov, A.; Giazitzoglou, E.; Siontis, G.C.; Po, S.S.; Camm, A.J.; Ioannidis, J.P.A. Autonomic denervation added to pulmonary vein isolation for paroxysmal atrial fibrillation: A randomized clinical trial. *J. Am. Coll. Cardiol.* **2013**, *62*, 2318–2325. [CrossRef] [PubMed]
189. Avazzadeh, S.; McBride, S.; O'brien, B.; Coffey, K.; Elahi, A.; O'halloran, M.; Soo, A.; Quinlan, L.R. Ganglionated Plexi Ablation for the Treatment of Atrial Fibrillation. *J. Clin. Med.* **2020**, *9*, 3081. [CrossRef] [PubMed]
190. Zheng, N.; Fu, Y.; Xue, F.; Xu, M.; Ling, L.; Jiang, T. Which ablation strategy is the most effective for treating persistent atrial fibrillation? A systematic review and Bayesian network meta-analysis of randomized controlled trials. *Heart Rhythm* **2025**, *22*, e60–e73. [CrossRef] [PubMed]
191. Aksu, T.; Skeete, J.R.; Huang, H.H. Ganglionic Plexus Ablation: A Step-by-step Guide for Electrophysiologists and Review of Modalities for Neuromodulation for the Management of Atrial Fibrillation. *Arrhythmia Electrophysiol. Rev.* **2023**, *12*, 2023. [CrossRef] [PubMed]
192. Benabou, L.; Ascione, C.; Soré, B.; Cherbi, M.; Labrousse, R.; Tixier, R.; Bouyer, B.; Arnaud, M.; Buliard, S.; Pambrun, T.; et al. A computed tomography–based evaluation and comparison of ganglionated plexus targeting techniques for cardioneuroablation. *Heart Rhythm*, 2025; *in press*. [CrossRef] [PubMed]

193. Wang, S.; Fang, R.; Huang, L.; Zhou, L.; Liu, H.; Cai, M.; Sha'aBan, A.; Yu, C.; Akkaif, M.A. Acupuncture in Traditional Chinese Medicine: A Complementary Approach for Cardiovascular Health. *J. Multidiscip. Healthc.* **2024**, *17*, 3459–3473. [CrossRef] [PubMed]
194. Kim, J.H.; Jung, H.J.; Kim, T.H.; Lee, S.; Kim, J.E.; Kang, K.W.; Jung, S.Y.; Kim, A.R.; Park, H.J.; Shin, M.S.; et al. Auricular acupuncture for prehypertension and stage 1 hypertension: Study protocol for a pilot multicentre randomised controlled trial. *Trials* **2013**, *14*, 303. [CrossRef] [PubMed]
195. Zhou, W.; Ko, Y.; Benharash, P.; Yamakawa, K.; Patel, S.; Ajijola, O.A.; Mahajan, A. Cardioprotection of electroacupuncture against myocardial ischemia-reperfusion injury by modulation of cardiac norepinephrine release. *Am. J. Physiol.-Heart Circ. Physiol.* **2012**, *302*, H1818–H1825. [CrossRef] [PubMed]
196. Ma, L.; Cui, B.; Shao, Y.; Ni, B.; Zhang, W.; Luo, Y.; Zhang, S. Electroacupuncture improves cardiac function and remodeling by inhibition of sympathoexcitation in chronic heart failure rats. *Am. J. Physiol.-Heart Circ. Physiol.* **2014**, *306*, H1464–H1471. [CrossRef] [PubMed]
197. Huang, Y.; Lu, S.-F.; Hu, C.-J.; Fu, S.-P.; Shen, W.-X.; Liu, W.-X.; Li, Q.; Wang, N.; He, S.-Y.; Liang, F.-R.; et al. Electro-acupuncture at Neiguan pretreatment alters genome-wide gene expressions and protects rat myocardium against ischemia-reperfusion. *Molecules* **2014**, *19*, 16158–16178. [CrossRef] [PubMed]
198. Longhurst, J. Acupuncture's cardiovascular actions: A mechanistic perspective. *Med. Acupunct.* **2013**, *25*, 101–113. [CrossRef] [PubMed]
199. Zhao, L.; Li, D.; Zheng, H.; Chang, X.; Cui, J.; Wang, R.; Shi, J.; Fan, H.; Li, Y.; Sun, X.; et al. Acupuncture as Adjunctive Therapy for Chronic Stable Angina: A Randomized Clinical Trial. *JAMA Intern. Med.* **2019**, *179*, 1388–1397. [CrossRef] [PubMed]
200. Lin, Y.; Wang, X.; Li, X.-B.; Wu, B.-Q.; Zhang, Z.-H.; Guo, W.-H.; Wu, C.-C.; Chen, X.; Chen, M.-L.; Dai, Z.; et al. Acupuncture for persistent atrial fibrillation after catheter ablation: Study protocol for a pilot randomized controlled trial. *Trials* **2021**, *22*, 35. [CrossRef] [PubMed]
201. Kimura, K.; Kitagawa, Y.; Tajima, F. Effects of a Single Session of Acupuncture Treatment on Blood Pressure and Heart Rate Variability in Patients with Mild Hypertension. *J. Altern. Complement. Med.* **2021**, *27*, 342–348. [CrossRef] [PubMed]
202. Wang, Q.; Liang, D.; Wang, F.; Li, W.; Han, Y.; Zhang, W.; Xie, Y.; Xin, W.; Zhou, B.; Sun, D.; et al. Efficacy of electroacupuncture pretreatment for myocardial injury in patients undergoing percutaneous coronary intervention: A randomized clinical trial with a 2-year follow-up. *Int. J. Cardiol.* **2015**, *194*, 28–35. [CrossRef] [PubMed]
203. Ni, X.; Xie, Y.; Wang, Q.; Zhong, H.; Chen, M.; Wang, F.; Xiong, L. Cardioprotective effect of transcutaneous electric acupoint stimulation in the pediatric cardiac patients: A randomized controlled clinical trial. *Paediatr. Anaesth.* **2012**, *22*, 805–811. [CrossRef] [PubMed]
204. Abdi, H.; Tayefi, M.; Moallem, S.R.; Zhao, B.; Fayaz, M.; Ardabili, H.M.; Razavi, A.-A.; Darbandi, M.; Darbandi, S.; Abbasi, P.; et al. Abdominal and auricular acupuncture reduces blood pressure in hypertensive patients. *Complement. Ther. Med.* **2017**, *31*, 20–26. [CrossRef] [PubMed]
205. Chunling, G.; Kai, C.; Shouqin, Y.; Shaofeng, R.; Hengyap, T.; Xiaofeng, G.; Dandan, P. Efficacy on rabbits with arrhythmia: Needling acupoint of Neiguan (PC6) at shallow or deep depth, and retaining needles for 10, 20, or 30 min. *J. Tradit. Chin. Med.* **2021**, *41*, 968–973.
206. Sun, Q.; Cheng, K.; Dai, X.; Yang, Z.; Wu, X.; Xu, C.; Qiu, X.; Gao, X.; Liu, D.; Yang, Q. Effect of electroacupuncture at Neiguan (PC6) at different time points on myocardial ischemia reperfusion arrhythmia in rats. *J. Tradit. Chin. Med.* **2024**, *44*, 113–121.
207. Zuo, H.; Cui, S.; Wang, K.; Wu, X.; Zhou, J.; Qu, Q.; Tong, Y.; Wu, S.; Zhou, M. Electroacupuncture Ameliorates Acute Myocardial Ischemic Injury and Long QT Interval in Mice through the α1A-Adrenergic Receptor: Electrophysiological, Morphological, and Molecular Evidence. *Oxidative Med. Cell. Longev.* **2022**, *2022*, 1984706. [CrossRef] [PubMed]
208. Yin, J.; Yang, M.; Yu, S.; Fu, H.; Huang, H.; Yang, B.; Liu, Y.; He, B.; Bao, M.; Wu, G.; et al. Effect of acupuncture at Neiguan point combined with amiodarone therapy on early recurrence after pulmonary vein electrical isolation in patients with persistent atrial fibrillation. *J. Cardiovasc. Electrophysiol.* **2019**, *30*, 910–917. [CrossRef] [PubMed]
209. Lomuscio, A.; Belletti, S.; Battezzati, P.M.; Lombardi, F. Efficacy of acupuncture in preventing atrial fibrillation recurrences after electrical cardioversion. *J. Cardiovasc. Electrophysiol.* **2011**, *22*, 241–247. [CrossRef] [PubMed]
210. Markman, T.M.; Pothineni, N.V.K.; Zghaib, T.; Smietana, J.; McBride, D.; Amankwah, N.A.; Linn, K.A.; Kumareswaran, R.; Hyman, N.; Arkles, J.; et al. Effect of transcutaneous magnetic stimulation in patients with ventricular tachycardia storm: A randomized clinical trial. *JAMA Cardiol.* **2022**, *7*, 445–449. [CrossRef] [PubMed]
211. Norise, C.; Hamilton, R.H. Non-invasive Brain Stimulation in the Treatment of Post-stroke and Neurodegenerative Aphasia: Parallels, Differences, and Lessons Learned. *Front. Hum. Neurosci.* **2016**, *10*, 675. [CrossRef] [PubMed]
212. Sheen, J.Z.; Miron, J.-P.; Mansouri, F.; Dunlop, K.; Russell, T.; Zhou, R.; Hyde, M.; Fox, L.; Voetterl, H.; Daskalakis, Z.J.; et al. Cardiovascular biomarkers of response to accelerated low frequency repetitive transcranial magnetic stimulation in major depression. *J. Affect. Disord.* **2022**, *318*, 167–174. [CrossRef] [PubMed]

213. Gulli, G.; Tarperi, C.; Cevese, A.; Acler, M.; Bongiovanni, G.; Manganotti, P. Effects of prefrontal repetitive transcranial magnetic stimulation on the autonomic regulation of cardiovascular function. *Exp. Brain Res.* **2013**, *226*, 265–271. [CrossRef] [PubMed]
214. Rast, J.; Sohinki, D.; Warner, A. Non-invasive Neuromodulation of Arrhythmias. *J. Innov. Card. Rhythm. Manag.* **2024**, *15*, 5757–5766. [CrossRef] [PubMed]
215. Wang, S.; Zhou, X.; Wang, Z.; Huang, B.; Zhou, L.; Chen, M.; Yu, L.; Jiang, H. Magnetic fields in noninvasive heart stimulation: A novel approach for anti-atrial fibrillation. *Int. J. Cardiol.* **2015**, *190*, 54–55. [CrossRef] [PubMed]
216. Yu, L.; Dyer, J.W.; Scherlag, B.J.; Stavrakis, S.; Sha, Y.; Sheng, X.; Garabelli, P.; Jacobson, J.; Po, S.S. The use of low-level electromagnetic fields to suppress atrial fibrillation. *Heart Rhythm* **2015**, *12*, 809–817. [CrossRef] [PubMed]
217. Sohinki, D.; Thomas, J.; Scherlag, B.; Stavrakis, S.; Yousif, A.; Po, S.; Dasari, T. Impact of low-level electromagnetic fields on the inducibility of atrial fibrillation in the electrophysiology laboratory. *Heart Rhythm* O_2 **2021**, *2*, 239–246. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.