Acupuncture after valve surgery is feasible and shows promise in reducing post-operative atrial fibrillation: The ACU-HEART pilot trial

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PII: S2666-2736(23)00124-9
DOI: https://doi.org/10.1016/j.xjon.2023.05.010
Reference: XJON 789

To appear in: JTCVS Open

Received Date: 20 February 2023
Accepted Date: 9 May 2023


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The feasibility and efficacy of daily acupuncture after valve surgery: ACU-Heart randomized pilot trial

- 3.8 (±1.1) sessions delivered per patient
- 83% ACU delivery rate
- Well tolerated
- No safety concerns
- 58% reduction in POAF
- Reductions in post-op pain, nausea, stress and anxiety

Incidence of POAF by group.

Daily acupuncture after valve surgery is feasible, well tolerated, and shows promise in reducing post-operative pain, nausea, stress and anxiety and incidence of POAF. A larger multicenter trial is warranted.

ACU=acupuncture group, SC=standard control group, POAF=post-operative atrial fibrillation.
Acupuncture after valve surgery is feasible and shows promise in reducing post-operative atrial fibrillation: The ACU-HEART pilot trial

Abbreviated title: ACU-Heart pilot trial

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Patil MD⁵, Tatyana Shafiro³, Ania Grimone³, Fang Lin³, Charles J. Davidson MD⁴, Melinda
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Accepted for poster presentation at the 103rd AATS Annual Meeting scheduled May 6-9, 2023

Disclosure Statement:
KLF: Nothing to disclose.
JTM: Nothing to disclose.
CE: Nothing to disclose.
ACA: Nothing to disclose.
DV: Nothing to disclose.
JK: Nothing to disclose.
VG: Nothing to disclose.
KDP: Boston Scientific, consultant.
TS: Nothing to disclose.
AG: Nothing to disclose.
FL: Nothing to disclose.
CJD: Edwards Lifesciences grant support and uncompensated consultant; Abbott, grant support.
MR: Nothing to disclose.
PMM: Atricure and Medtronic, honorarium; Abbott, advisory board; Edward Lifesciences,
royalties and consulting.

Informed Consent: This pilot study was approved by the Institutional Review Board of
Northwestern University (IRB#: STU00201408, approved 6/6/17). Participants provided written
informed consent which included permission for publication.
Funding Statement: This pilot study was funded by a philanthropic gift from the Malkin Family Foundation and the sponsor had no participation in the study design, collecting, analyzing, and interpreting the data, writing the report, or deciding whether and where to submit for publication.

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Word Count: 3357
Glossary of Abbreviations:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACU</td>
<td>acupuncture intervention</td>
</tr>
<tr>
<td>AF</td>
<td>atrial fibrillation</td>
</tr>
<tr>
<td>PNSA</td>
<td>pain, nausea, stress, anxiety</td>
</tr>
<tr>
<td>POAF</td>
<td>post-operative atrial fibrillation</td>
</tr>
<tr>
<td>POD</td>
<td>post-operative day</td>
</tr>
<tr>
<td>SC</td>
<td>standard care</td>
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</tbody>
</table>
Central Picture Legend: Daily inpatient acupuncture was associated with a decreased incidence of in-hospital POAF.

Central Message:

ACU-Heart evaluated daily acupuncture after valve surgery. Primary endpoint of feasibility was met, as were secondary endpoints of reduced POAF incidence and post-surgical symptoms.

Perspective Statement:

ACU-Heart is a randomized controlled pilot trial (n=100) of daily acupuncture or standard care following valve surgery that demonstrates the feasibility and potential benefit of post-operative acupuncture in the cardiac surgical setting. Acupuncture was well tolerated, without adverse effects, and positively impacted patients’ symptoms. Reduced incidence of POAF is promising.

Abstract

Objective: Acupuncture is an effective treatment for arrhythmias and post-operative symptoms but has not been investigated after cardiac surgery. Acupuncture After Heart Surgery (ACU-Heart) is a prospective, randomized, controlled pilot trial of daily inpatient acupuncture (ACU) or standard care (SC) following valve surgery with the primary endpoint being feasibility and secondary endpoints being reduction in POAF incidence and post-operative symptoms.

Methods: 100 patients without history of AF underwent primary valve surgery via sternotomy, randomized 1:1 to ACU (51) or SC (49). ACU patients received daily inpatient sessions starting POD1. Post-operative symptoms (pain, nausea, stress, anxiety) were assessed once daily in SC
and pre/post daily intervention in ACU. The groups were comparable except for age (ACU: 55.6±11.4, SC: 61.0±9.3; p=.01).

Results: ACU-Heart met primary and secondary endpoints. There were no adverse events. An average of 3.8(±1.1) ACU sessions were delivered per patient, during a mean 4.6(±1.3)-day hospital stay. ACU was associated with a reduction in pain, nausea, stress and anxiety after each session (p<.0001) and ACU patients had reduced post-op stress and anxiety across admission compared to SC (p=.049 and p=.036, respectively). ACU was associated with reduced POAF incidence [ACU: 7(13.7%), SC:16(32.7%); p=.028], fewer discharges on amiodarone [ACU: 5(9.8%), SC: 13(26.5%); p=.03], and fewer hours in the ICU (ACU: 30.3±10.0, SC: 37.0±22.5; p=.057).

Conclusions: Acupuncture after valve surgery is feasible, well tolerated and has clinical benefit. The reduction noted in POAF incidence will inform larger trials designed to further investigate the impact of ACU on POAF and medical outcomes.

Keywords: Acupuncture; post-operative atrial fibrillation; cardiac surgery; valve surgery; clinical trial
Introduction

Post-operative atrial fibrillation (POAF) is one of the most common complications after cardiac surgery, impacting anywhere from 10% to 65% of patients, depending on type of surgery, surveillance, and patient characteristics, with a higher incidence following valve surgery.\textsuperscript{1-3} POAF places considerable burden on the health care system, contributing to stroke and increased hospital and late mortality.\textsuperscript{4, 5} Effective therapy to reduce POAF remains elusive but welcome, given its impact on morbidity, mortality and health care costs.

Acupuncture may prove to be a promising prophylactic treatment after heart surgery, with potential to curtail POAF while also reducing surgical side effects, such as pain, nausea, and post-operative anxiety.\textsuperscript{6-10} Previous studies have shown that stimulation of the PC 6 point (located on the anterior forearm, Figure 1) has an antiarrhythmic effect in patients with persistent and paroxysmal atrial fibrillation (AF), with acupuncture intervention associated with comparable recurrence rates when compared to amiodarone up to a year after cardioversion.\textsuperscript{11, 12} In a 2017 systematic review and meta-analysis comprising 13 randomized controlled trials with a total of 797 participants, the authors concluded that acupuncture was as effective as traditional antiarrhythmic medications for treating arrhythmias (Risk Ratio [RR]: 1.18, 95% Confidence Interval [CI]: 0.78-1.79, $p=0.44$), and acupuncture was superior to no treatment (RR: 18.80, 95% CI: 12.68-24.92, $p<.001$).\textsuperscript{13} While daily acupuncture has yet to be examined after cardiac surgery or in the context of POAF, one time use of preoperative or intra-operative acupuncture during heart surgery has demonstrated anesthetic, pain mitigating, and anti-arrhythmic properties of acupuncture, resulting in decreased pulmonary infection, opioid consumption, postoperative nausea and emesis, and health care costs.\textsuperscript{9, 14-16} Acupuncture for postoperative pain management
has proven beneficial across a variety of surgical populations, contributing to decreased pain severity, opioid use, and opioid-related side-effects.\textsuperscript{7,16-19}

To our knowledge, the feasibility of daily acupuncture in the hospital setting following open heart surgery has not yet been established, but acupuncture offers promise in reducing incidence of POAF and severity of post-operative pain, nausea, and anxiety. We set out to close this gap by devising an acupuncture protocol that has potential to improve postoperative outcomes. The Acupuncture After Heart Surgery (ACU-Heart) pilot trial was designed with the primary endpoint of feasibility. Secondary endpoints were incidence of POAF, severity of post-operative pain, nausea, stress, and anxiety (PNSA), and medical outcomes. ACU-Heart investigators limited this pilot trial to valve surgery patients given the traditionally higher incidence of POAF following valve surgery,\textsuperscript{1} in an attempt to maximize statistical power amidst a smaller sample.

\textbf{Methods}

\textit{Study Design}

ACU-Heart was a prospective, two-arm, randomized, feasibility pilot trial examining the use of daily postoperative acupuncture among patients recovering from valve surgery. Eligible patients were approached during a pre-operative clinic visit for non-emergent valve surgery. Patients were assigned randomly (1:1) to Acupuncture intervention (ACU) or Standard Care (SC) following informed consent, completion of questionnaires, and a scheduled surgical date. Those randomized to receive ACU were offered daily intervention beginning postoperative day (POD) 1 and continuing until discharge or POD 6.
During postoperative hospitalization, patients completed self-report ratings of PNSA, once daily in SC and twice daily in ACU, immediately before and after intervention to allow for pre-post comparison. PNSA for both groups were completed within the same time window. Participants in ACU were queried 3 months postoperatively about perceived benefit of post-operative acupuncture. See Supplemental Figure 1 for study design flow.

Recruitment and Eligibility

Eligible patients were ≥18 years old with valvular disease, scheduled for non-emergent valve surgery via sternotomy after evaluation in the cardiac surgery clinic of a large Midwestern tertiary academic medical center between January 2016 and August 2019. Patients were ineligible to participate if they had a history of AF or flutter, prior or concomitant cardiac surgery, and/or presented with pre-surgical or post-surgical conditions unfavorable for acupuncture. To evaluate the impact of acupuncture on new onset POAF, participants were excluded if they developed AF intra-operatively or prior to the start of intervention (afternoon of POD1).

Ethics and Informed Consent

This study was approved by the Institutional Review Board of Northwestern University (IRB#: STU00201408, approved 6/6/17). Participants provided written informed consent which included permission for publication.

Randomization
Patients were randomly assigned (1:1) to ACU or SC via sealed envelopes containing study arm assignment generated by the study statistician who was not involved in enrollment. Participants were notified of randomization status the morning of surgery.

**Surgical Protocol**

In accordance with STS performance criteria, patients received pre-operative beta blockers. No other AF prophylaxis was performed. Postoperative AF was treated similarly in both groups, according to STS protocol, with amiodarone plus cardioversion as needed. Patients received continuous telemetry monitoring until discharge.

**Acupuncture Intervention**

The study intervention was a novel application of established acupuncture practice, administered in the hospital setting to patients recovering from valve surgery. The ACU-Heart acupuncture protocol consisted of 9 acupoints that were utilized in each session (5 on the body, 4 on the ear), chosen to target common symptoms after heart surgery, including arrhythmias, mood disturbance, pain, nausea, and stress (Table 1). Each acupuncture session began with a formal assessment consistent with Traditional Chinese Medicine (TCM). At the start of each intervention, the acupuncturist had the freedom to add additional acupoints from the ACU-Heart supplemental acupoints protocol, in accordance with TCM practice and based on the TCM assessment and patient presentation.
Single-use sterile SEIRIN (0.16x15 and 0.16x30) needles were inserted ¼ to 1 inch, depending on location and underlying anatomy, and no manipulation nor stimulation was delivered. Once in place, needles were retained by the patient for approximately 30 minutes. Weekday acupuncture sessions occurred late afternoon/evening and weekend sessions occurred midday. Nursing staff were notified of the timing in advance. Intervention occurred in the patient’s private hospital room, either in bed or in a bedside recliner, depending on patient and nursing preference. Efforts were made to minimize interruptions and maintain a quiet space.

Three licensed acupuncturists trained in TCM provided acupuncture intervention and are employed by the Osher Center for Integrative Health at the same academic institution. Each had prior experience delivering acupuncture in the medical setting and underwent training to gain familiarity with the postoperative cardiac surgery setting and to ensure consistency across providers and sessions. Acupuncturists were not blinded to treatment condition.

**Standard Care**

Participants randomized to SC received no intervention.

**Data collection**

Outcome measures:

**Feasibility.** Feasibility of the intervention was assessed via acceptability and intervention delivery. Acceptability examined enrollment, retention, intervention tolerance, adverse events, and patient feedback. Intervention delivery examined completed, missed, and interrupted sessions.
POAF. POAF was determined via an adjudication committee consisting of one electrophysiologist and two cardiac surgeons who reviewed each patient chart to ascertain the presence of POAF during hospitalization, in accordance with the Society of Thoracic Surgeons (STS). Raters were blinded to treatment condition and to each other’s ratings. Unanimous consensus was required. Discrepancies (2) were discussed until consensus reached.

_Pain, Nausea, Stress, Anxiety (PNSA)._ Patients rated current severity of PNSA each on a scale of 0 to 10, once daily in SC and twice daily in ACU, before and after acupuncture. Acupuncturists were blinded to PNSA ratings.

_Acupuncture History and Expectations._ A self-report measure captured history of acupuncture use and expectations related to postoperative acupuncture.

_Intervention Feedback._ Patients rated the helpfulness of each acupuncture session on a scale of 0 to 100. Acupuncturists were blinded to ratings. At 3-months post-op, patients were asked, “Overall, did you find acupuncture after heart surgery to be helpful?” with response options ranging from 0 to 4.

_Medical information._ Pre-operative, intra-operative and post-operative data were pulled directly from our patient population in the STS database. This includes demographics, cardiac disease etiology, co-morbidities, risk factors, surgical details, concomitant procedures, complications, and length of stay (LOS) in the intensive care unit (ICU) and hospital.

_Statistical Methods_
The primary objective of this pilot trial was to evaluate the feasibility of post-operative acupuncture via enrollment, retention, safety, and intervention delivery. A secondary objective was to obtain an initial estimate of the effect size of acupuncture on targeted endpoints, thus informing the design of a larger and more definitive future clinical trial. Secondary endpoints included medical outcomes (POAF, LOS, complications) and post-surgical PNSA. Being hypothesis-generating, this pilot trial was not powered to detect specific differences in POAF between groups. However, within each arm, 50 participants was estimated to provide over 90% power to detect a POAF incidence as low as 4.5% at 0.025 significance level.

Participant enrollment, retention, completed interventions, missed interventions, interrupted interventions, patient feedback and baseline characteristics were summarized using mean±standard deviation, median/interquartile range values, or counts/percentages, as appropriate. Surgical outcome measures, including POAF, LOS, complication rates, and use of antiarrhythmic therapies, were summarized and compared using exact test for binomial proportions, Chi-square test, Fisher’s exact test, or Wicoxon’s rank sum test, depending on data distributions. Longitudinal measures of post-op symptoms were analyzed via linear mixed effects models and generalized estimating equation. Within group comparisons of pre- and post-acupuncture symptoms were based on paired t-tests or Wilcoxon’s signed rank test. Statistical significance was declared at two-sided 5% level and no adjustments for multiple testing were made. All statistical analyses were performed in SAS v. 9.4 (SAS Institute, Cary, NC).

**Results**

Table 2 includes demographic and clinical characteristics by study arm. Participants were predominantly male (71%), Caucasian (86%), and college educated (71%). Average age was
58.3(±10.7) years. Participants underwent surgical correction of the mitral valve (68%), aortic valve (35%), and/or tricuspid valve (4%; Table 3). The two groups were well balanced except for age (SC: 61.0±9.3 years, ACU: 55.6±11.4 years, p=.01). A majority of participants (73%) reported no prior acupuncture history. Of those with prior experience (n=27), 82% had received 5 or fewer sessions, primarily for pain management.

Primary Feasibility Endpoint

Acceptability

Enrollment and Retention. Two hundred fifty-five consecutive patients were deemed eligible to participate in ACU-Heart during a pre-op clinic visit. 146 (57%) provided consent and 45 (17.6%) declined. Reasons for declining included: disinterest in research (36%), disinterest in acupuncture (31%), feeling overwhelmed by surgery (22%), and other (11%). Sixty-four patients approached were lost to follow-up, 39 of whom were later determined to be ineligible and 25 of whom retained eligibility but never consented nor declined (“passive decliners”). Of the 146 who consented to participate, 12 were excluded prior to randomization for no longer meeting inclusionary criteria and 31 were excluded after randomization for meeting ineligibility during the pre- or peri-operative course. Primary reason for post-randomization exclusion was concomitant surgery. Three withdrew participation, 2 prior to intervention and 1 after intervention began. This participant received 2 ACU sessions and withdrew citing pain after returning to the ICU for placement of ICD. These 3 participants formally withdrew consent to be included in the study and thus are not retained in the final sample, but are noted here for purposes of acceptability. Thus, for purposes of outcomes of this pilot trial, the final sample is comprised of 100 participants (51 ACU, 49 SC). Aside from the 1 patient who withdrew after
intervention began, 100% who received intervention were retained in the study at hospital discharge and 96% of ACU responded to the 3-month follow-up (See Figure 2 CONSORT diagram for details).

**Participant Feedback.** Participants rated daily acupuncture as beneficial overall, with an average rating of 69.0±26.6 on a scale of 0-100. At follow-up, participants reflected that acupuncture was moderately helpful [35 (74.4%)], with an additional 8 (17.0%) reporting it was extremely helpful and 4 (8.5%) reporting no perceived benefit.

**Intervention Tolerance and Adverse Events.** Acupuncture was well tolerated, as demonstrated by adherence to the study protocol. All needles were retained for the entirety of the intervention. No adverse events were reported. One complaint occurred in real time when a participant felt a pinch on her arm when a blood pressure cuff inflated close to a needle. The needle was repositioned with no further complaint.

**Intervention Delivery**

Delivery of acupuncture intervention proved logistically feasible in both the cardiac surgery ICU and the step-down unit. In fact, 100% of ACU patients received acupuncture on POD1 in the cardiac surgery ICU. ACU patients received an average of 3.8(±1.1) acupuncture sessions across an average length of stay of 4.7(±1.5) days. Missed sessions were uncommon. Of a total of 230 sessions that could have been delivered across the entirety of the study, 192 were completed, an 83% completion rate. Majority of the missed sessions occurred on day of discharge, which had a 43% completion rate.

Interruptions occurred during 22 sessions (11%) and included: nurse entry (11), phone rang (5), visitor entry (2), physician entry (2), hallway noise (1) and bathroom needs (1). Despite interruptions, the intervention was completed according to protocol 100% of the time. Ten
sessions were conducted while the TV was on, 1 was conducted with music on, and 1 session was delivered while patient was wearing a CPAP mask.

Secondary Outcomes

Secondary endpoint analyses revealed a statistically significant antiarrhythmic effect for acupuncture. As shown in Figure 3, new onset POAF occurred in 23% of the overall sample, with reduced incidence among those in ACU (7, 13.7%) versus those in SC (16, 32.7%, p=.028). Discharge on amiodarone followed the same pattern, with 5 (9.8%) ACU patients and 13 (26.5%) SC patients discharged on the antiarrhythmic (p=.03). Participants in ACU spent fewer hours in the ICU compared with SC, a trend approaching statistical significance (p=.057), but total LOS was comparable between groups. The groups were comparable regarding other complications. Operative characteristics and outcomes are displayed in Table 3.

Secondary endpoint analyses revealed a significant benefit to post-operative PNSA. Daily stress and anxiety levels across hospital admission were more favorable in ACU vs. SC (stress: F=3.91, p=.049; anxiety: F=4.46, p=.036). Within ACU, PNSA severity were each significantly reduced following intervention, compared with pre-session levels. (p<.0001; Figure 4).

Discussion

The ACU-Heart pilot trial successfully demonstrated that postoperative daily acupuncture in the hospital setting following valve surgery is feasible and efficacious, associated with reduced incidence of POAF, decreased need for amiodarone at discharge, shorter ICU LOS, and reductions in postoperative PNSA (Figure 5).
The primary endpoint of feasibility was met. Daily acupuncture following valve surgery was well received by patients and logistically feasible. Retention was high. Three withdrawals occurred, all in ACU, implying potential patient hesitation towards acupuncture during surgical recovery. However, the majority of patients (73%) had no prior experience with acupuncture, suggesting that openness to postoperative acupuncture is not dependent on prior history. Acupuncture delivery was feasible in both the ICU and the surgical step-down unit, with 100% of ACU patients receiving intervention on POD1. Intervention proved more difficult to deliver on day of discharge, not surprisingly, but maintained a high rate of delivery overall (83%).

Patients not only accepted and tolerated acupuncture after valve surgery, but most found it to be a positive experience.

ACU-Heart met secondary endpoints of improved outcomes, as noted by reductions in incidence of POAF and severity of postoperative PNSA. Those receiving acupuncture experienced a 58% reduction of incidence of POAF compared with those in SC. The antiarrhythmic properties of acupuncture previously found in the outpatient setting among those with persistent and paroxysmal AF\textsuperscript{11,12} may extend to POAF, offering a safe and noninvasive prophylaxis option for POAF. At a cost of about $280 per surgical patient in this trial, acupuncture is a relatively inexpensive adjunct therapy with potential to reduce health care costs. Post-operative symptoms also improved from acupuncture. The benefit to pain control may extend to pulmonary recovery, as acupuncture-mediated pain reduction has been shown to enhance lung functioning after cardiac surgery.\textsuperscript{15} Together, these findings suggest that acupuncture has a promising future in the cardiac surgery setting.
The post-surgical environment is fast-paced and the feasibility of adding 30-45 minutes daily for acupuncture intervention was unknown. ACU-Heart demonstrated that acupuncture delivery can be well integrated into the cardiac surgery setting. Minor hospital intrusions did not impede intervention delivery. The success of intervention delivery is in part attributed to the flexibility and support of the acupuncturists and nursing staff. Acupuncturists were available 7 days a week. Nursing staff worked to minimize interruptions. Despite potential for this intervention to feel burdensome to providers, nurses often commented that they observed a positive change in patient disposition following a session. The potential benefit of acupuncture to patients’ mood and pain could strengthen staff support and further promote intervention delivery.

The specific mechanism(s) for acupuncture-mediated rhythm control and pain reduction are not yet well understood but several physiological pathways may exist, including anti-inflammatory, release of endogenous opioids, and autonomic mechanisms related to vagal or sympathetic neural activity. In a study that found amiodarone plus acupuncture superior to an amiodarone-only control group among patients with persistent AF undergoing pulmonary vein isolation, those who received acupuncture exhibited lower inflammatory markers including TNF-alpha, IL-6, CRP, TGF-beta1, and MMP2. Future trials will benefit from incorporating markers of inflammation and sympathetic arousal to better elucidate mechanistic pathways.

While ACU-Heart successfully executed a novel approach to post-operative cardiac recovery, it is not without several limitations. First, there was an imbalance in age between groups despite randomization, where those in SC were slightly older and spent more minutes on cardiopulmonary bypass, two factors that could contribute to increased POAF. These imbalances
are not ideal but do not detract from the primary endpoint of feasibility. Interpretation of secondary endpoints are preliminary and require a larger trial to understand more definitely the role of acupuncture on surgical outcomes. However, the incidence of POAF in ACU (13.7%) is lower than expected and likely not uniquely reflective of sample characteristics. Second, results may be limited in generalizability due to the narrow inclusion criteria of the study. Several participants became ineligible post-randomization. In retrospect, randomization would have been ideal post-surgery when it was evident that participants still met inclusion criteria. We chose not to perform intent-to-treat analyses with all participants randomized given this would create significant heterogeneity that could undermine meaningful results in this size sample (e.g., including those who did not undergo surgery, underwent concomitant surgery, etc). As a pilot trial with primary endpoint of feasibility, we felt comfortable proceeding with analyses as planned, utilizing those retained in the final sample after all exclusionary criteria were met.

ACU-Heart utilized chart review limited to the surgical admission for detection of POAF, limiting our understanding of acupuncture’s impact on timing and severity of POAF, including post-discharge complications, readmission rates, and later-onset or recurrence of POAF.

Acupuncturists and patients were not blinded to randomization which may have impacted patients’ self-report of symptoms. A comparison group of SC was chosen given our goal of assessing feasibility. Sham acupuncture interventions are largely viewed as suboptimal in the integrative medicine community, with potential for false negative results due to incidental factors of sham acupuncture, which is not considered fully inert. Adding an attention control arm or sham acupuncture arm may be useful in future studies so long as a SC control can help discern differences due to treatment-related factors (e.g., acupuncture) versus incidental factors (e.g., uninterrupted time).
ACU-Heart demonstrates the successful integration of a novel acupuncture intervention into cardiac surgery recovery that benefits surgical outcomes and postoperative symptoms. This trial demonstrates that, with close cooperation with the acupuncture team, postoperative acupuncture is feasible and beneficial. Acupuncture was safe. The important secondary endpoints demonstrating reduced incidence of POAF, more favorable outcomes, and improved postsurgical symptoms were met. A larger randomized trial of patients undergoing a variety of cardiac operations in multiple medical centers is warranted. In addition to clinical results, examination of potential underlying physiologic mechanisms is warranted.

**Conclusion**

The increased morbidity, mortality and health care burden imparted by POAF following valve surgery warrants ongoing consideration of alternate treatment strategies. Acupuncture after valve surgery proves to be a feasible and well tolerated adjunct therapy that shows promise in reducing POAF and post-surgical PNSA. To our knowledge, this was the first study to assess the feasibility and acceptability of daily acupuncture in the hospital setting following heart surgery. A larger multicenter trial targeting a broader surgical population is warranted to evaluate the impact of acupuncture on the severity and timing of POAF, as well as to investigate physiological mechanisms.

**Acknowledgments**

ACU-Heart is funded by a philanthropic gift from the Malkin Family Foundation. The support and generosity of the Malkin family are greatly appreciated.
References


Table 1. ACU-Heart acupuncture protocol plus supplemental acupoints.

<table>
<thead>
<tr>
<th>ACU-Heart acupuncture protocol: Acupoints utilized in every ACU session:</th>
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</thead>
<tbody>
<tr>
<td><strong>Body acupoints and associated targeted symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>PC 6</td>
<td>atrial fibrillation, nausea, anxiety, depression</td>
</tr>
<tr>
<td>HT 7</td>
<td>atrial fibrillation, anxiety, depression</td>
</tr>
<tr>
<td>LI 4</td>
<td>pain, depression</td>
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<tr>
<td>LIV 3</td>
<td>pain, depression</td>
</tr>
<tr>
<td><strong>Yin Tang</strong></td>
<td>anxiety, depression</td>
</tr>
<tr>
<td><strong>Auricular (Ear) acupoints and associated targeted symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>Shen Men</td>
<td>anxiety, depression, pain, insomnia, inflammation</td>
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<tr>
<td>Sympathetic</td>
<td>smooth muscle spasms, anxiety, blood circulation, pain</td>
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<tr>
<td>Heart (C)</td>
<td>chest pain, angina, arrhythmia, blood pressure</td>
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<tr>
<td>Point Zero</td>
<td>homeostasis, anxiety, depression</td>
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<table>
<thead>
<tr>
<th>ACU-Heart supplemental acupoints: Additional acupoints available for use each session in response to the daily TCM assessment and symptom presentation:</th>
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</thead>
<tbody>
<tr>
<td><strong>Depression:</strong></td>
<td>UB 3 point was added if patient reported depression</td>
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<tr>
<td></td>
<td>o Optional body points: LU 9, SP 6, DU 20</td>
</tr>
<tr>
<td></td>
<td>o Optional auricular points: Antidepressant, Brain, Master Cerebral</td>
</tr>
<tr>
<td><strong>Anxiety:</strong></td>
<td>UB 3 point was added if patient reported anxiety</td>
</tr>
<tr>
<td></td>
<td>o Optional auricular points: Master Cerebral, Brain, Cingulate Gyrus</td>
</tr>
<tr>
<td><strong>Nausea:</strong></td>
<td>ST 36 point was added if patient reported nausea</td>
</tr>
<tr>
<td></td>
<td>o Optional body points: SP 6, CV 12</td>
</tr>
<tr>
<td></td>
<td>o Optional auricular points: Cardiac Orifice, Vagus nerve</td>
</tr>
<tr>
<td><strong>Pain:</strong></td>
<td>SP 10 and GB 34 points were added if patient reported pain</td>
</tr>
<tr>
<td></td>
<td>o Optional body point: TW 5</td>
</tr>
<tr>
<td></td>
<td>o Optional auricular points: Brain, Tranquilizer Point, 1 point corresponding to location of pain</td>
</tr>
</tbody>
</table>

ACU, acupuncture; PC, Pericardium meridian; HT, Heart meridian; LI, Large Intestine meridian; LIV, Liver meridian; TCM, Traditional Chinese Medicine; UB, Bladder meridian; LU, Lung meridian; SP, Spleen meridian; DU, Governing vessel; ST, Stomach meridian; CV, Conception vessel; GB, Gallbladder meridian; TW, Triple Warmer.
### Table 2. Baseline clinical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Entire Cohort (N=100)</th>
<th>ACU (N=51)</th>
<th>SC (N=49)</th>
<th>P value</th>
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<td>100</td>
<td>58.3 (±10.7)</td>
<td>55.6 (±11.4)</td>
<td>61.0 (±9.3)</td>
<td>.011</td>
</tr>
<tr>
<td>Female</td>
<td>100</td>
<td>29 (29%)</td>
<td>15 (29%)</td>
<td>14 (29%)</td>
<td>.926</td>
</tr>
<tr>
<td>Race – White</td>
<td>100</td>
<td>86 (86%)</td>
<td>44 (86%)</td>
<td>42 (86%)</td>
<td>.097</td>
</tr>
<tr>
<td>Body mass index</td>
<td>100</td>
<td>27.4±5.2</td>
<td>27.0±5.3</td>
<td>26.9±5.0</td>
<td>.332</td>
</tr>
<tr>
<td>CHADS&lt;sub&gt;2&lt;/sub&gt; score</td>
<td>100</td>
<td>0.7±0.8</td>
<td>0.6±0.7</td>
<td>0.8±0.9</td>
<td>.198</td>
</tr>
<tr>
<td>Creatinine level</td>
<td>100</td>
<td>1.0 (0.9, 1.0)</td>
<td>1.0 (0.9, 1.1)</td>
<td>1.0 (0.9, 1.0)</td>
<td>.704</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>100</td>
<td>65.0 (61.5, 69.0)</td>
<td>65.0 (60.0, 67.0)</td>
<td>65.9 (63.0, 69.0)</td>
<td>.137</td>
</tr>
<tr>
<td>Left atrial size</td>
<td>100</td>
<td>4.0 (3.7, 4.7)</td>
<td>4.0 (3.9, 4.9)</td>
<td>4.0 (3.7, 4.6)</td>
<td>.416</td>
</tr>
<tr>
<td>Diabetes</td>
<td>100</td>
<td>6 (6.0%)</td>
<td>1 (2.0%)</td>
<td>5 (10.2%)</td>
<td>.083</td>
</tr>
<tr>
<td>Current smoker</td>
<td>100</td>
<td>3 (3.0%)</td>
<td>2 (3.9%)</td>
<td>1 (2.0%)</td>
<td>.582</td>
</tr>
<tr>
<td>Renal failure</td>
<td>100</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>.702</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>100</td>
<td>46 (46%)</td>
<td>24 (47.1%)</td>
<td>22 (44.9%)</td>
<td>.828</td>
</tr>
<tr>
<td>Hypertension</td>
<td>100</td>
<td>45 (45%)</td>
<td>22 (43.1%)</td>
<td>23 (46.9%)</td>
<td>.702</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>100</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>.702</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>100</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>.702</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>100</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>.702</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>100</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td>.305</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>97</td>
<td>2 (2.1%)</td>
<td>0 (0%)</td>
<td>2 (4.3%)</td>
<td>.132</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>100</td>
<td>10 (10%)</td>
<td>4 (7.8%)</td>
<td>6 (12.2%)</td>
<td>.463</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>91</td>
<td>6 (6.6%)</td>
<td>3 (6.5%)</td>
<td>3 (6.7%)</td>
<td>.978</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation, n (%), or median (interquartile range). ACU= acupuncture arm; SC, standard control arm; LVEF, left ventricular ejection fraction; CHADS<sub>2</sub>, congestive heart failure, hypertension, age, diabetes, gender.
Table 3. Intra-operative and post-operative outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Entire Cohort (N=100)</th>
<th>ACU (N=51)</th>
<th>SC (N=49)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve surgery</td>
<td>100</td>
<td>68 (68%)</td>
<td>34 (66.7%)</td>
<td>34 (69.4%)</td>
<td>.771</td>
</tr>
<tr>
<td>MV repair</td>
<td>100</td>
<td>65 (65.0%)</td>
<td>33 (64.7%)</td>
<td>32 (65.3%)</td>
<td></td>
</tr>
<tr>
<td>MV replacement</td>
<td>100</td>
<td>3 (3.0%)</td>
<td>1 (2.0%)</td>
<td>2 (4.1%)</td>
<td></td>
</tr>
<tr>
<td>Aortic valve surgery</td>
<td>100</td>
<td>35 (35%)</td>
<td>17 (33.3%)</td>
<td>18 (36.7%)</td>
<td>.721</td>
</tr>
<tr>
<td>AV repair</td>
<td>100</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
<td>2 (11.1%)</td>
<td></td>
</tr>
<tr>
<td>AV replacement</td>
<td>100</td>
<td>33 (33%)</td>
<td>17 (33.3%)</td>
<td>16 (32.7%)</td>
<td></td>
</tr>
<tr>
<td>Tricuspid valve surgery</td>
<td>100</td>
<td>4 (4.0%)</td>
<td>2 (3.9%)</td>
<td>2 (4.1%)</td>
<td>.967</td>
</tr>
<tr>
<td>ASD/PFO surgery</td>
<td>100</td>
<td>7 (7.0%)</td>
<td>3 (5.9%)</td>
<td>4 (8.2%)</td>
<td>.655</td>
</tr>
<tr>
<td>Cardiopulmonary bypass (min)</td>
<td>100</td>
<td>80.7 (±19.1)</td>
<td>76.9 (±16.8)</td>
<td>84.7 (±20.7)</td>
<td>.039</td>
</tr>
<tr>
<td>Cross clamp time (min)</td>
<td>100</td>
<td>69.1 (±17.4)</td>
<td>65.9 (15.6)</td>
<td>72.4 (±18.7)</td>
<td>.061</td>
</tr>
<tr>
<td>ICU length of stay, hours</td>
<td>100</td>
<td>33.6 (±17.5)</td>
<td>30.3 (±10.0)</td>
<td>37.0 (±22.5)</td>
<td>.057</td>
</tr>
<tr>
<td>Total length of stay, days</td>
<td>100</td>
<td>4.6 (±1.3)</td>
<td>4.7 (±1.5)</td>
<td>4.5 (±1.0)</td>
<td>.597</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>100</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
<td>2 (4.1%)</td>
<td>.145</td>
</tr>
<tr>
<td>Post-operative stroke</td>
<td>100</td>
<td>2 (2.0%)</td>
<td>2 (3.9%)</td>
<td>0 (0%)</td>
<td>.161</td>
</tr>
<tr>
<td>POAF</td>
<td>100</td>
<td>23 (23%)</td>
<td>7 (13.7%)</td>
<td>16 (32.7%)</td>
<td>.028</td>
</tr>
<tr>
<td>Discharged on amiodarone</td>
<td>100</td>
<td>18 (18%)</td>
<td>5 (9.8%)</td>
<td>13 (26.5%)</td>
<td>.030</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation, n (%). ACU, acupuncture arm; SC, standard control arm; MV, mitral valve; AV, aortic valve; ASD (PFO), atrial septal defect (patent foramen ovale); ICU, intensive care unit; POAF, post-operative atrial fibrillation.
Figure 1. Locations of 3 of the 9 ACU-Heart acupoints utilized in each acupuncture session. The PC 6 point has been shown to have anti-arrhythmic properties. PC, Pericardium meridian; HT, Heart meridian.
Figure 2. Enrollment Flow Chart. 255 patients were approached for the study, 146 of whom consented to participate. An additional 45 declined and 64 were lost to follow-up. After further exclusion of 12 patients who no longer met study criteria, 134 were randomized 1:1 to standard control (SC) or daily acupuncture (ACU). 31 patients (17 SC, 14 ACU) were excluded after randomization for meeting exclusionary criteria peri-operatively. 3 patients withdrew from the study, all in ACU. The final sample consisted of 100 patients (49 SC, 51 ACU). SC, standard control arm; ACU, acupuncture intervention arm.
Figure 3. Incidence of POAF and discharge on amiodarone by group. Patients in ACU had a lower incidence of POAF compared to those in SC (13.7% vs. 32.7%, p=0.028). Fewer patients in ACU were discharged on amiodarone (9.8% vs 26.5%, p=0.03). ACU, acupuncture intervention arm; POAF, post-operative atrial fibrillation, SC, standard control arm;.
**Figure 4.** Severity of post-operative symptoms before and after acupuncture among the ACU participants. Pain, nausea, stress and anxiety were each reduced following daily acupuncture intervention, both with each day (p<0.001) and collapsed across days (p<0.001). PNSA, self-reported rating of pain, nausea, stress, anxiety; ACU, acupuncture intervention arm.
The feasibility and efficacy of daily acupuncture after valve surgery: ACU-Heart randomized pilot trial

Patients in ACU begin acupuncture on POD1; receive daily sessions up to POD6

100 valve surgery patients randomized 1:1 to daily acupuncture (ACU, 51) or standard care (SC, 49)

Hospital discharge

3 months post-op

Assess pain, nausea, stress, anxiety; once daily (SC) or twice daily (ACU)

Assess helpfulness of acupuncture (ACU)

Footnote: Locations of 3 of the 9 ACU-Heart acupoints utilized in each acupuncture session. The PC 6 point has been shown to have anti-arrhythmic properties.

- 3.8 (±1.1) sessions delivered per patient
- 83% ACU delivery rate
- Well tolerated
- No safety concerns
- 58% reduction in POAF
- Reductions in post-op pain, nausea, stress and anxiety

Incidence of POAF by group.

Daily acupuncture after valve surgery is feasible, well tolerated, and shows promise in reducing post-operative pain, nausea, anxiety and incidence of POAF. A larger multicenter trial is warranted.

ACU=acupuncture group; SC=standard control group; POAF=post-operative atrial fibrillation.

Figure 5. The ACU-Heart pilot trial. Postoperative daily acupuncture in the hospital setting following valve surgery is feasible and efficacious, associated with reduced incidence of POAF, shorter ICU LOS, and reductions in postoperative PNSA.
Supplemental Figure 1. Study Design Flow. Eligible patients were approached and consented at a pre-operative clinic visit, at which time they completed baseline questionnaires. Patients in ACU received daily acupuncture starting on POD1. Daily assessments of PNSA were completed daily in SC and pre- and post- acupuncture in ACU. Patients in ACU completed a questionnaire about the post-operative acupuncture experience at 3 months post-op. ACU, acupuncture intervention arm; SC, standard control; POD1, post-operative day 1; PNSA, self-report rating of pain, nausea, stress and anxiety.
**Bar Chart**

**POAF Incidence**
- **SC**: 32.7
- **ACU**: 13.7

**Percentage of Participants**

- **P = 0.028**
**Approached:**
255 patients

**Declined:**
45 patients
- not interested in research (36%)
- not interested in acupuncture/fear of needles (31%)
- too stressed about surgery (22%)
- and other (11%)

**Lost to follow-up:**
64 patients
- Remained eligible (25)
- Did not remain eligible (39)

**Consented:**
146 patients

**Excluded:**
12 patients
- did not complete study measures (4)
- concomitant surgery (3)
- non-sternotomy approach (1)
- no surgery (2)
- medical comorbidity (1)
- research conflict (1)

**Randomized:**
134 patients

**SC:**
66 patients

**Excluded:**
31 patients
- 17 SC | 14 ACU
- concomitant surgery (SC 6, ACU 4)
- intra-op AF (SC 2, ACU 2)
- POAF before POD1 (SC 2, ACU 3)
- non-sternotomy approach (SC 1, ACU 1)
- did not undergo surgery (SC 2, ACU 1)
- team error (SC 1, ACU 2)
- medical exclusion (SC 3, ACU 1)

**ACU:**
68 patients

**Withdrawn:**
3 patients
- 0 SC | 3 ACU

**Final SC sample:**
49 patients

**Final ACU sample:**
51 patients
Daily acupuncture after valve surgery is feasible, well tolerated, and shows promise in reducing post-operative pain, nausea, stress and anxiety. A larger multicenter trial is warranted.
P=0.028

P=0.03

32.7

13.7

26.5

9.8

POAF Incidence

Discharged on Amiodarone

Percentage of Participants

SC  ACU
Patient consented during pre-op clinic visit

Patient undergoes valve surgery

Patient in ACU begins acupuncture on POD1 and receives up to 6 daily sessions

PNSA Assessment: Once daily (SC) or before and after each acupuncture session (ACU); patient feedback (ACU)

Hospital discharge

3 months post-op

Assessment of benefit of acupuncture (ACU)