Commentary

Does acupuncture reduce the risk of acute myocardial infarction?

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A R T I C L E   I N F O

1. Focal article

Chuang SF, Shih CC, Yeh CC, Lane HL, Tsai CC, Chen TL, Lin JG, Chen T, Liao CC. Decreased risk of acute myocardial infarction in stroke patients receiving acupuncture treatment: A nationwide matched retrospective cohort study. BMC Complement Altern Med 2015;15:318.

2. Aim

To compare the risk of acute myocardial infarction (AMI) during follow-up between an acupuncture exposure group and a nonexposure group of stroke patients.

3. Study design and data source

A nationwide retrospective cohort study was conducted. The data source was the Taiwan National Health Insurance Research Database, which was established in 1995 and covers 99% of residents in Taiwan.

4. Study population

For this study, 182,619 new-onset stroke survivors aged 40–79 years who were hospitalized primarily because of stroke were screened. The admission dates ranged from January 2000 to December 2004. Among those screened, 23,475 patients who received at least one acupuncture treatment course (i.e., six continuous acupuncture treatments) were selected.

5. Exposure (acupuncture) and nonexposure group

The ratio of the exposure to the nonexposure group was 1:2

(1) Exposure group: 23,475 patients who received at least one acupuncture treatment course.
(2) Nonexposure group: 46,950 patients who did not receive acupuncture treatment were matched according to propensity score, with a 0.2 standard deviation of the log odds scale for propensity scores.

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6. Follow-up duration

Follow-up time was calculated as person-years until AMI diagnosis. To avoid immortal time bias, the time from hospital discharge to the first acupuncture treatment was defined as the immortal time.

(1) Exposure group: followed up from the first acupuncture treatment date until December 31, 2009, or censored.
(2) Nonexposure group: followed up from the discharge date after stroke until December 31, 2009, or censored.

7. Confounding factors

Age, sex, income, stroke subtype, coexisting medical condition (hypertension, diabetes, mental disorder, traumatic brain injury, hyperlipidemia, cardiac arrhythmia, Parkinson's disease, depression, Alzheimer's disease, obesity, and malignant brain tumors), hospital stay length, undergoing neurosurgery, intensive care unit admission, cardiovascular medication (antiplatelet, lipid-lowering agent, and anticoagulant), smoking cessation, and rehabilitation.

8. Main outcome measures

Adjusted hazard ratio analyzed using the multivariate Cox proportional hazard model.

9. Main results

(1) No significant differences were observed between the exposure and nonexposure groups in terms of all the confounding factors at baseline.

(2) Risk of AMI: The stroke patients in the exposure (acupuncture) group had a lower incidence of AMI than those in the nonexposure group (9.2 per 1000 person-years vs. 10.8 per 1000 person-years). The adjusted hazard ratio was 0.86 [95% confidence interval (CI), 0.80–0.93].

(3) Dose-response relationship in acupuncture treatment: Increase in the number of acupuncture treatment sessions was associated with a reduced risk of AMI. A dose-response relationship was also observed. The HR of the risk of AMI of the patients who received more than 15 acupuncture treatment courses was 0.61 (95% CI, 0.51–0.73). AMI incidence reduced from 11.2 to 6.7 per 1000 person-years (Table 1).

10. Authors' conclusions

The stroke patients who received acupuncture treatments seemed to have a lower risk of AMI than those who did not receive acupuncture treatments.

11. Comment/critique

Even though this nationwide cohort study was preliminary, it demonstrated that acupuncture seemed to reduce the risk of AMI in stroke patients. A dose-response relationship was observed. In the original article, the authors suggested several possible explanations.[1] Firstly, according to a previous research study, acupuncture treatment enhanced the physical movement capacity of stroke patients. As higher cardiorespiratory fitness and physical activity are inversely correlated with the risk of AMI,[2] AMI risk reduction of stroke patients in the acupuncture group is reasonable. The authors also explained that the heart rate reduction effect,[3] lipid profile-lowering effect,[4] antidepressant effect,[5] and increased

No. of acupuncture treatment course	Events	Person-y	Incidence[*]	HR	95% CI[†]
0	2,978	265,756	11.2	1.00	(reference)
≥1	1,054	106,663	9.9	0.86	(0.80–0.93)
≥2	733	81,701	9.0	0.79	(0.73–0.86)
≥3	550	66,789	8.2	0.73	(0.67–0.80)
≥4	449	56,537	7.9	0.71	(0.64–0.78)
≥5	374	49,103	7.6	0.68	(0.61–0.76)
≥6	330	43,027	7.7	0.69	(0.62–0.77)
≥7	276	38,333	7.2	0.65	(0.58–0.74)
≥8	249	34,381	7.2	0.66	(0.58–0.75)
≥9	220	31,218	7.0	0.64	(0.56–0.74)
≥10	199	28,312	7.0	0.64	(0.56–0.74)
≥11	184	26,153	7.0	0.64	(0.55–0.74)
≥12	169	24,206	7.0	0.64	(0.55–0.75)
≥13	151	22,417	6.7	0.62	(0.52–0.73)
≥14	143	20,854	6.9	0.63	(0.53–0.77)
≥15	130	19,545	6.7	0.61	(0.51–0.73)

Table 1 – Number of acupuncture treatments and risk of acute myocardial infarction in stroke patients.

p (Cochran–Armitage test) < 0.0001.
[*] Per 1000 person-years.
[†] Adjusted for confounding factor.
  CI, confidence interval; HR, hazard ratio.

nitric oxide production by acupuncture were also related to the results.[6] Moreover, patients who were treated with acupuncture had better knowledge and attitude regarding rehabilitation and disease prevention.[1]

This study has several strengths such as the large patient sample, use of propensity scores for matching an untreated control group, adjustment for confounding factors by using the Cox proportional hazard model, and reduction of time-dependent bias regarding immortal time.[1] However, this study has several limitations. The authors mentioned the lack of information about the prescribed acupoints and procedure, lifestyle, family history of AMI, mental disorder, laboratory findings, stroke severity, and low estimation of stroke as limitations. Along with these, the study has several other limitations. Firstly, the results cannot be generalized owing to the inclusion criteria (stroke patients). Secondly, immobility due to a severe stroke was not investigated. In their paper, the authors did not describe whether acupuncture treatment was administered to inpatients or outpatients. However, it is reasonable that most of the acupuncture sessions were conducted for outpatients. Saczynski et al[7] reported that the length of hospitalization was 5.0 days in 2005. We can presume that patients who have limited mobility owing to severe stroke might not visit an acupuncture clinic. Thus, we cannot exclude the possibility that immobility due to stroke, which might act as confounding factor, was more severe in the non-exposure group. Next, prior ischemic heart disease (IHD) was not investigated. In patients with acute coronary syndrome, major cardiovascular diseases (CVD) recur about 5% to 8% within 6 months.[8] Thus, distribution of prior IHD between the two groups should be identified. Finally, even though the effect of expectancy of acupuncture treatment on clinical outcomes is controversial,[9] expectation should be investigated.

The results of this cohort study are consistent with those of previous clinical trials and meta-analysis about IHD. For short-term surrogate outcome, Yang et al[10] reported that 5 days of consecutive electroacupuncture pretreatment prior to heart valve replacement surgery reduced the severity of cardiac ischemia-reperfusion injury. A similar cardioprotective effect was reported by Ni et al[11] that bilateral transcutaneous electrical acupoint (PC6) stimulation reduced serum cardiac troponin I level after congenital heart defect repair surgery. A clinical outcome study also showed better outcome in an acupuncture treatment group. Wang et al[12] reported that electrical acupoint stimulation reduced the myocardial infarction rate after percutaneous coronary intervention during 2 years of follow-up (50.0% vs. 30.4%, $p = 0.004$). In a systematic review about angina pectoris, the "acupuncture plus antiangina" medication group showed better electrocardiographic improvement than the medication-only group (risk ratio, 0.50; 95% CI, 0.40–0.62).[13] Therefore, acupuncture treatment is expected to show a beneficial effect in IHD patients.[14]

We can speculate that several factors influence the effectiveness of acupuncture treatment. In the original article, the acupuncture effects did not differ according to sex or stroke subtype. However, an interesting point was that acupuncture treatment showed a dose-response relationship with clinical outcome. In retrospective research, only relationships, not causality, can be identified. However, a dose-response relationship is a required condition to consider causality.[15]

Thus, it is meaningful and essential to identify the dose-response relationship for causality. In a meta-analysis of 17,922 individual patients with chronic pain, the number of acupuncture sessions correlated with better outcome ($\beta = 0.11$; 95% CI, 0.01–0.21).[16] Other factors, such as electrical stimulation and treatment duration, also influenced outcome in terms of chronic pain.[16] Acupoint specificity is important in CVD. PC5-PC6 and ST36-ST37 are considered important acupoints in CVD.[14] An interesting acupuncture clinical trial protocol about point specificity in patients with stable angina pectoris was registered by Li et al[17]. Patient age is also an important factor. In the subgroup analysis of the original article, acupuncture had no effect in patients older than 70 years. The authors explained that older patients have more comorbidities that reduce the effect of acupuncture. Mechanism is also important. In a recent acupuncture trial for hypertension, baseline plasma norepinephrine and renin levels were higher in the responder group than in the nonresponder group.[18] The factors that predict responders to acupuncture from among patients with CVD might be identified by performing a retrospective cohort or observational study.

The next step in future acupuncture trials for IHD is conducting a prospective observational study. A comparison between randomized controlled trials and observational data showed that the predictability of appropriately analyzed observational data on cardiovascular events were good enough (Spearman coefficient, 0.73; $p < 0.001$).[19] A proof-of-concept study about the effects of acupuncture that evaluates infarct size reduction based on creatine kinase-MB level, troponin I level, and cardiac magnetic resonance and echocardiographic parameters is also needed. The final goal of acupuncture trials for IHD is to conduct a large clinical outcome study with a cost-effective analysis.

Conflicts of interest

None declared.

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