Biostatistik

Du er blevet udset som ekspert i biostatistik af editoren for *The Journal of Maternal-Fetal & Neonatal Medicine*. Han vil gerne have dine kommentarer på et par passager i en artikel. For hvert afsnit har editoren nogle spørgsmål til Metode, Resultat og Konklusions afsnittene, som du bedes besvare og begrunde alle dine svar med fx overvejelser, mellemregninger, skitser etc.

Introduktionen er vedlagt for at give overblik. Af eksamenstekniske grunde er dele af artiklen fjernet og en kommentar indsat. De 10 spørgsmål vægtes med hver 5 % i forbindelse med bedømmelsen.

Introduction

In 2002, 7% of all deliveries occurred after 42 weeks of gestation[1] (or 294 days). Post-term pregnancies are known to be at greater risk for fetal and maternal morbidity and mortality…

[Her var en lang række fordele ved ikke at føde for sent].

Acupuncture is gaining acceptance in Western societies as a treatment for several pregnancy indications. There do not appear to be any significant maternal or fetal risks of acupuncture…

[Her var en række fortræffeligheder ved akupunktur].

We set out to evaluate whether outpatient[2] acupuncture treatments combined with routine medical care can shorten the time to delivery, reduce rates of labor induction or decrease rates of cesarean section[3] in term, nulliparous[4] women as compared to routine medical care alone.

Methods

This study was conducted in an outpatient clinical setting at the University of North Carolina (UNC) Family Medicine Center from July 2004 through February 2005. The study protocol was approved by the Biomedical Investigational Review Board at the UNC School of Medicine, and all subjects provided informed written consent to participate on the date of enrollment.

Potentially eligible women were identified by prenatal[5] chart review and recruited by the principal investigator via telephone. Eligible and interested women were scheduled for their first study visit, at which time the principal investigator (T.H.) administered both a digital cervical[6] examination and an ultrasound to document fetal[7] presentation and placental[8] location.

A list of random numbers was generated by using the software program, Stata Version 8 (Stata Corporation, College Station, TX, USA) with equal proportions of blocks of two and four.

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[1] Graviditet
[2] Ambulant
[3] Kejsersnit
[4] Førstegangsfødende
[5] Før-fødsel
[6] I denne sammenhæng livmoderhals
[7] Foster
[8] Moderkage

Numbered, sealed, manila envelopes contained the group assignment and were opened by the principal investigator after all entry criteria were confirmed. Women were allocated to receive the acupuncture protocol along with routine medical care (acupuncture group) or routine medical care alone (control group). Care providers and patients were not blinded to the treatment arm assignment.

Acupuncture treatments were administered on three out of four consecutive days starting with the day of enrollment.

[Her var en masse detaljer om hvordan akupukkturen er givet.]

Patients allocated to the control group received routine medical care and were evaluated for a follow-up study visit three to four days following enrollment. There were no provider or patient restrictions to continued medical care in either group (e.g., membrane sweeping, timing of inductions or herbal supplementation for cervical ripening). Baseline (day of enrollment) and final (day 3 or 4) measurements were performed in both groups and included cervical examination and documentation of Bishop score[9].

The primary outcome measure was time elapsed from randomization to delivery. Secondary outcomes included mode of delivery, frequency of spontaneous labor, and neonatal[10] complications. Additionally, change in Bishop score and cervical dilation were assessed in both groups. We used Student's *t*-test to compare means of continuous variables and Chi-square analysis to compare categorical outcomes. Survival analyses were performed using the Kaplan-Meier test for equality of survivors. Two-sided *p*-values less than or equal to 0.05 were considered statistically significant. All charts were reviewed by an investigator who was blinded to treatment arm assignment throughout data abstraction.

Spørgsmål til metode afsnittet

1) Hvilke etiske overvejelser har forfatterne gjort sig inden forsøget? Er forsøget etisk forsvarligt?
2) Er forsøget korrekt randomiseret og blændet?
3) Hvilken type studie er der tale om?

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[9] Ens score der beskriver om fødslen skal sættes i gang
[10] Nyfødt

Results

Two hundred and thirty-five women were screened for eligibility. Of these, 139 (58%) delivered prior to enrollment, 33 (14%) declined participation, and seven (3%) did not reach eligibility criteria. Fifty-six nulliparous women were randomized, 30 to the acupuncture group and 26 to the control group (Figure 2). All patients completed their assigned treatment (unless delivery occurred) except for one woman in the acupuncture group who attended only two of her three acupuncture sessions. No patient abbreviated their treatment course secondary to discomfort during the procedures. Complete delivery outcome data were available on all women. There were no significant differences between the two groups in the demographic or medical measures assessed (Table I). The natural course of some of the pregnancies in each group was truncated by induction of labor in 22/56 (39%) of all cases (30% of the acupuncture group and 50% of the control group).

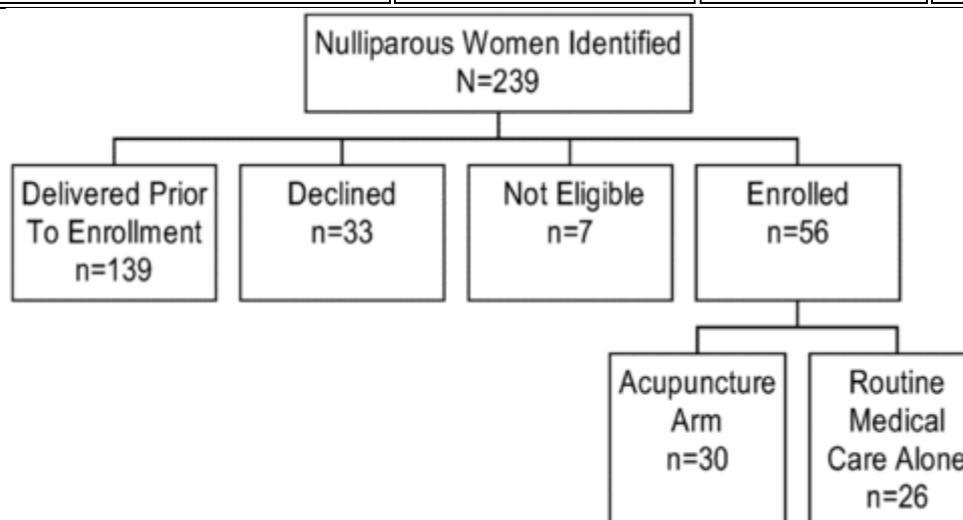| Table I. Demographic and clinical characteristics.			
	Acupuncture (*n* = 30)	**Control (*n* = 26)**	***p*-Value**
Mean maternal age, years (SD)	29.2 (4.9)	29.1 (4.8)	0.91
Mean gestational age, weeks (SD)	40.13 (0.54)	40.13 (0.45)	0.49
Intake median Bishop score	4	4	0.20
Race/ethnicity (*n*)			
Caucasian	27	22	
Black	1	3	
Hispanic	2	1	0.46

Figure 2. Flow diagram of eligible patients.

Spontaneous labor occurred in 70% of women in the acupuncture group but only in 50% of controls (OR 2.33, 95% CI 0.78-6.98, *p* = 0.12).

[Her var en masse andre outcome measures der ikke var signifikant forskellige for de to grupper]

We performed survival analysis to further explore the between-group differences in time to delivery. First, we analyzed deliveries over time for the entire sample of 56 subjects. We then

repeated this analysis after excluding subjects whose course of pregnancy was not truncated by inpatient induction (Figure 3). This difference reached statistical significance for the spontaneous group ($p = 0.05$), but not the entire population ($p = 0.26$).
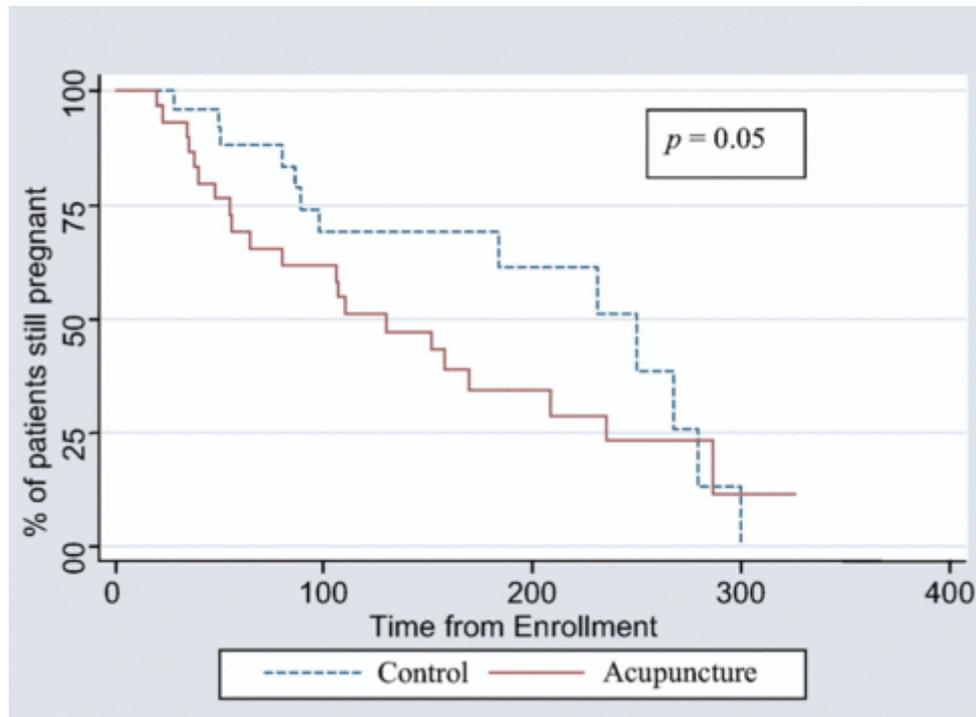

Figure 3.
Kaplan-Meier survival analysis of cumulative deliveries over time (spontaneous group only).

Spørgsmål til resultatafsnittet

4) Forskerne skriver: 'There were no significant differences between the two groups in the demographic…' Her hentyder de til etnicitet, men hvordan har de testet det? Hvorfor er det ikke korrekt at bruge denne test?
5) Hvad burde de have gjort?
6) Forskerne skriver: ' Spontaneous labor occurred in 70% of women in the acupuncture group but only in 50% of controls (OR 2.33, 95% CI 0.78-6.98, $p = 0.12$).' Hvordan er de kommet frem til en Odds Ratio på 2,33?
7) Hvordan er konfidensintervallet (CI) beregnet?
8) Forskerne har lavet en Kaplan-Meier test for at sammenligne fødselsraterne mellem kontrol og akupunktur gruppen (Figure 3). Hvordan skal figuren fortolkes?
9) Forskerne indikerer på figur 3 at der er en signifikant forskel, men hvilken test kan de have brugt?

Discussion

In this randomized clinical trial, we sought to evaluate the efficacy of acupuncture for outpatient labor initiation. The findings from our study are similar to those of the trial by Rabl. Both studies demonstrated that acupuncture was associated with a decrease in time from enrollment into the study to delivery, but the differences in our study did not reach statistical significance.

[Her var en argumentation om at det udførte forsøg var ok]

In summary, the findings from this study neither prove nor disprove that acupuncture is effective in initiating labor among nulliparous women at or near their due date. This study does, however, suggest that acupuncture is safe and well tolerated by women near the end of their pregnancy. The fact that all of the measures of efficacy (interval to delivery, spontaneous labor, and route of delivery) trended towards a favorable response suggests that outcomes potentially associated with acupuncture are more likely to be favorable than unfavorable.

This study clearly demonstrates that assessing the efficacy of acupuncture for the initiation of labor is feasible, but a larger sample size and the inclusion of a sham acupuncture comparison arm are needed. The findings do not provide sufficient evidence to support including acupuncture as part of routine prenatal care, however. A sham acupuncture comparison would control for several potential placebo effects while also masking perinatal healthcare providers to subjects' treatment arm allocation.

10) Kan resultaterne bære de fremførte konklusioner?