

## Gastric Emptying of Water in Term Pregnancy

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**Background:** Healthy nonpregnant patients may ingest clear liquids until 2 h before induction of anesthesia without adversely affecting gastric volume. The purpose of this study was to compare gastric emptying in term, nonlaboring pregnant women after ingestion of 50 ml water (control) with that after ingestion of 300 ml water.

**Methods:** Gastric emptying was assessed in healthy, non-obese, term pregnant volunteers using both serial gastric ultrasound examinations ( $n = 9$ ) and acetaminophen absorption ( $n = 11$ ) in a crossover study design. After an overnight fast, volunteers ingested 1.5 g acetaminophen and 50 or 300 ml water (assigned in random order) on two occasions separated by at least 2 days. Serial gastric antrum cross-sectional areas were determined using gastric ultrasound imaging, and the half-time to gastric emptying was calculated. Serial plasma acetaminophen concentrations were measured. Areas under the plasma acetaminophen concentration *versus* time curve, peak concentrations, and time to peak concentration for 50- and 300-ml ingestions were compared.

**Results:** Gastric emptying half-time was significantly shorter after ingestion of 300 ml water than after ingestion of 50 ml ( $24 \pm 6$  vs.  $33 \pm 8$  min). There were no differences in acetaminophen areas under the curve at 60, 90, or 120 min, or in acetaminophen peak concentration. Time to peak concentration of acetaminophen was significantly shorter after ingestion of 300 ml water than after ingestion of 50 ml ( $25 \pm 12$  vs.  $41 \pm 19$  min).

**Conclusions:** Gastric emptying in healthy, term, nonobese, nonlaboring pregnant women is not delayed after ingestion of 300 ml water compared with that after an overnight fast.

A RARE but sometimes fatal risk of anesthesia is pulmonary aspiration of gastric contents. Therefore, an empty stomach before the elective induction of anesthesia is desirable. Traditionally, patients have been asked to fast overnight to assure this goal. However, studies in healthy adults<sup>1-4</sup> and children<sup>5-7</sup> found little or no difference in gastric volumes or pH when comparing gastric volumes after a clear liquid fast of 2-3 h to a fast of 6 h or more. Therefore, guidelines for preoperative liquid ingestion have recently been liberalized.<sup>8</sup>

Gastric physiology during pregnancy may differ from that in nonpregnant individuals because of changes in hormone levels (e.g., progesterone and motilin) and displacement of the stomach by the gravid uterus. Recent studies of gastric emptying in nonlaboring term women,

using acetaminophen absorption,<sup>9,10</sup> applied tomography,<sup>11</sup> gastric impedance,<sup>12</sup> and ultrasonography,<sup>13</sup> suggest that gastric emptying is not delayed during pregnancy. The gastric emptying of clear liquids compared with emptying after an overnight fast in pregnant women at term has not been studied.

We hypothesized that gastric emptying in healthy, term, pregnant women after the ingestion of water would not differ from that observed in the same individuals after an overnight fast. The purpose of this study was to compare gastric emptying in healthy, nonobese, nonlaboring, term, pregnant volunteers after the ingestion of 50 ml water (control) with that after 300 ml water.

### Materials and Methods

Fifteen pregnant volunteers provided institutionally approved, written informed consent to participate in this crossover study. Exclusion criteria included systemic disease (including gestational diabetes mellitus), multiple gestation, prepregnancy body mass index greater than 30, use of medications known to affect gastric motility or secretion, and acetaminophen ingestion within 48 h of the study periods. Gastric emptying was determined directly by serial gastric ultrasound examinations<sup>14</sup> and indirectly using the acetaminophen (paracetamol) absorption method.<sup>15</sup>

Subjects were studied on two occasions, separated by at least 48 h, between 37 and 39 weeks' gestation. Subjects fasted overnight and presented for study participation at 7:30 AM. An intravenous catheter was inserted into a hand or arm vein. The catheter was attached to a disposable, pressurized, in-line flush system without heparin. This closed system allowed for return of the waste blood to the subject after each blood draw. A blank blood sample was drawn, and baseline ultrasound examination was performed. Study participants then ingested 1.5 g acetaminophen (15 ml clear liquid acetaminophen) immediately followed by 50 or 300 ml water, the order of which was randomized using a table of random numbers. Subjects remained in the semisitting position until completion of the serial ultrasound examinations and were then allowed to sit upright until the last blood sample was obtained.

Ultrasound examinations (Acuson, Mountain View, CA; 5-MHz probe) were performed by one of two ultrasonographers who were blinded to the volume of water ingested. The same ultrasonographer performed examinations on both occasions that a subject participated in

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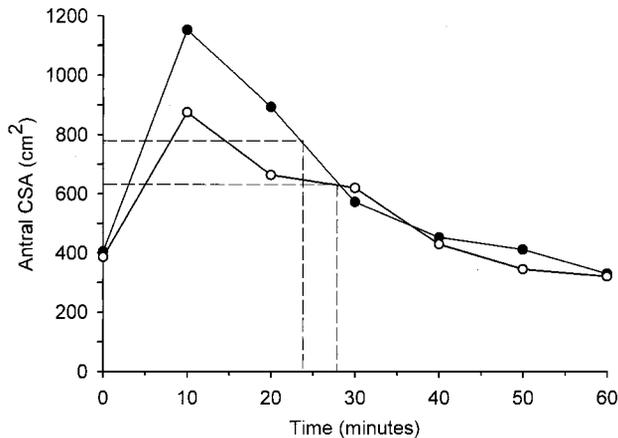


Fig. 1. Antral cross-sectional area (CSA) versus time for study subject no. 4. The dotted lines represent the calculation of half-time to gastric emptying. Open circle = 50 ml; filled circle = 300 ml.

the study. The subjects were positioned in a semiupright position with the head of the bed elevated to 45°. The gastric antrum was visualized at baseline and at 10-min intervals after acetaminophen ingestion for 60 min or until the cross-sectional area (CSA) returned to baseline. Correct identification of the stomach was confirmed by directly observing the entry of the study drug-water into the stomach.

The CSA of two sections of the gastric antrum (distal antrum near the pylorus [antrum<sub>pylorus</sub>] and proximal antrum, closer to the zone of transition between the corpus and antrum [antrum<sub>corpus</sub>]) were measured in two sagittal planes.<sup>14,17</sup> The maximal anteroposterior and longitudinal diameters were measured and the CSA for each antral section (corpus and pyloric) was calculated using the formula:

$$CSA = (AP)(L)\pi/4.$$

The antrum<sub>corpus</sub> and antrum<sub>pyloric</sub> CSAs at each time point were averaged for further data analysis. The half-maximal CSA (CSA<sub>1/2</sub>) was defined as follows:

$$CSA_{\text{maximum}} - [(CSA_{\text{maximum}} - CSA_{\text{baseline}})/2].$$

The half-time to gastric emptying (T<sub>1/2</sub>) was defined as the time from baseline until the antral CSA returned to the half-maximal value (fig. 1).<sup>18</sup>

Blood was drawn for determination of plasma acetaminophen concentrations before and every 10 min after ingestion of acetaminophen and water for 60 min, then every 30 min until 150 min after baseline. Plasma acetaminophen concentrations were measured using the high-performance liquid chromatographic technique of Ameer *et al.*,<sup>19</sup> except that samples were eluted isocratically at 1.2 ml/min using a mobile phase consisting of methanol-pH 5.29 0.05 M phosphate buffer in a 15:85 ratio after liquid-liquid extraction, using freshly pre-

pared acetylsalicylic acid as the internal standard. Using 0.25-ml plasma aliquots, this assay had a sensitivity of 0.5 µg/ml with within-day coefficients of variation of 5% or less. Areas under the acetaminophen concentration versus time curve were determined at 60, 90, and 120 min and on extrapolation to infinity by trapezoidal approximation. In addition, peak concentration and time to peak concentration were determined.

#### Statistical Analysis

A previous study using the gastric ultrasound method described above reported a T<sub>1/2</sub> of 24.8 ± 6.8 min for healthy adults after ingestion of beef broth.<sup>18</sup> Assuming baseline gastric emptying is not prolonged in pregnancy, power analysis (α = 0.05, power = 80%) determined that eight subjects would be necessary to show a clinically significant 100% increase in T<sub>1/2</sub> from baseline in a crossover study comparing gastric emptying after ingesting 50 ml of water (baseline) with that after ingestion of 300 ml of water.

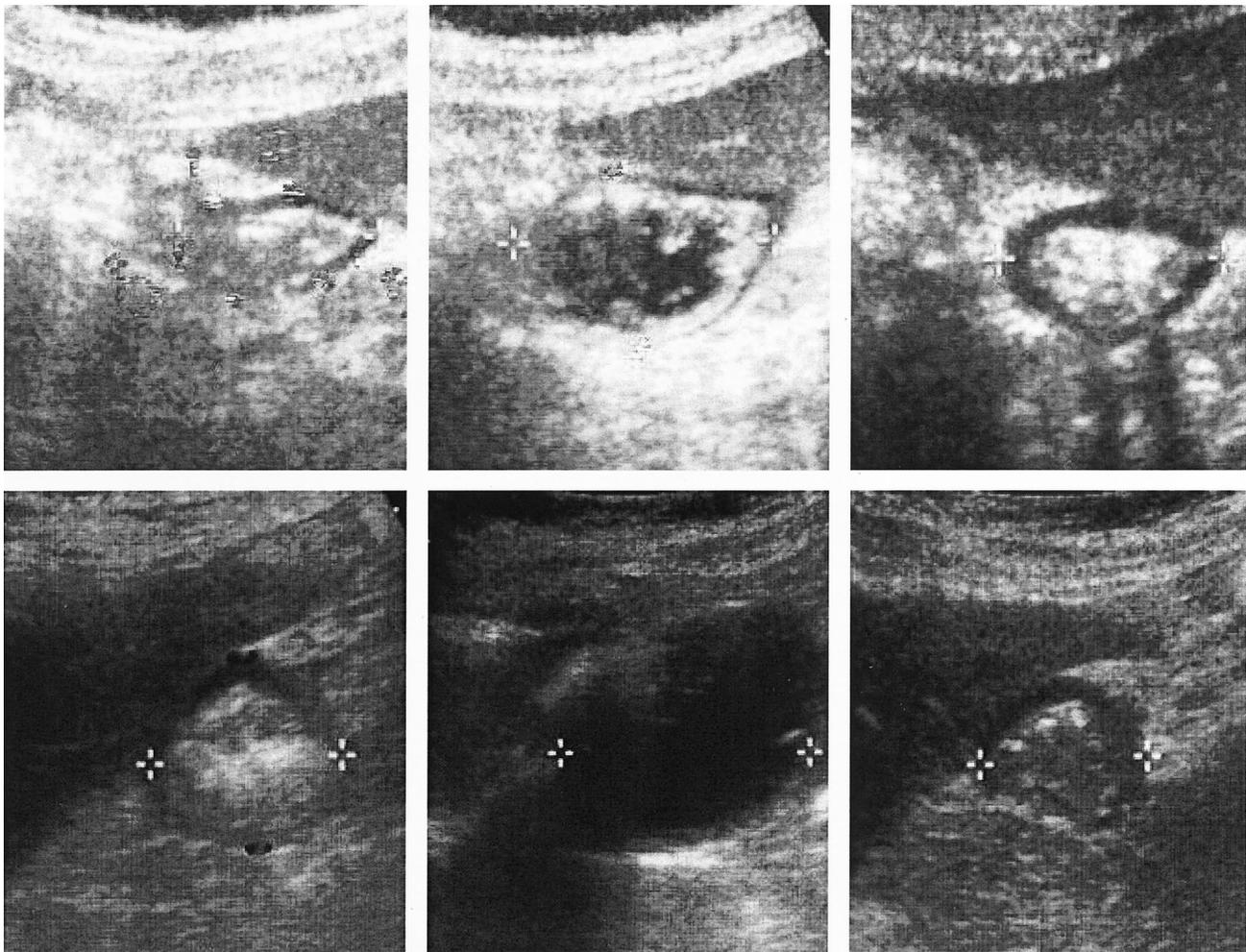
Data are summarized as mean ± SD. Control (50 ml) and treatment (300 ml) data were compared by two-tailed paired *t* tests. The criterion for rejection of the null hypothesis was *P* < 0.05.

## Results

Fifteen women volunteered to participate in the study. Four volunteers did not complete the study because they delivered their baby before the second study session could be conducted. A baseline ultrasound was not obtained for one subject, and a second subject (no. 12) was not monitored to CSA<sub>1/2</sub>, in violation of study protocol (see below). The ultrasound data from these subjects were excluded, and the complete ultrasound data from nine study subjects were analyzed. Ultrasound data from the nine study subjects were obtained for 60 min after baseline. Representative ultrasound images are presented in figure 2. The data from 11 volunteers who completed both study days were included in the acetaminophen data analysis. The characteristics of all 11 subjects are included in table 1.

The T<sub>1/2</sub> after ingestion of 300 ml water (24 ± 6 min) was significantly shorter than that after ingestion of 50 ml (33 ± 8 min) (*P* < 0.01; fig. 3). After ingestion of 300 ml water, mean CSA at 60 min was less than that at baseline.

Representative plasma acetaminophen concentration versus time relations for a single patient are presented in figure 4. The results of the analysis of the acetaminophen plasma concentration data are summarized in table 2. There were no differences in acetaminophen areas under the curves at 60, 90, or 120 min or on extrapolation to infinity, or in acetaminophen peak concentration.



**Fig. 2.** Sample anterior–posterior gastric ultrasound images for study subject no. 4 before and after ingestion of 50 (top) and 300 (bottom) ml water. Left = baseline; middle = 10 min; right = 60 min.

Time to peak acetaminophen concentration was significantly shorter after ingestion of 300 ml water than after 50 ml ( $25 \pm 12$  vs.  $41 \pm 19$  min).

After ingesting 50 ml water, study subject no. 12 had delayed gastric emptying, as evidenced by both the ultrasound and acetaminophen data. The CSA increased from  $901 \text{ cm}^2$  (baseline) to  $2,121 \text{ cm}^2$  at 10 min, decreased to  $1,755 \text{ cm}^2$  at 30 min, and then oscillated around this value for 20 min, but CSA had not decreased to CSA1/2 by 60 min, the time of the last ultrasound

measurement. Her time to peak acetaminophen concentration (90 min) was the longest of all the study subjects for both volumes of water, and her peak concentration ( $12.3 \mu\text{g/ml}$ ) was the lowest.

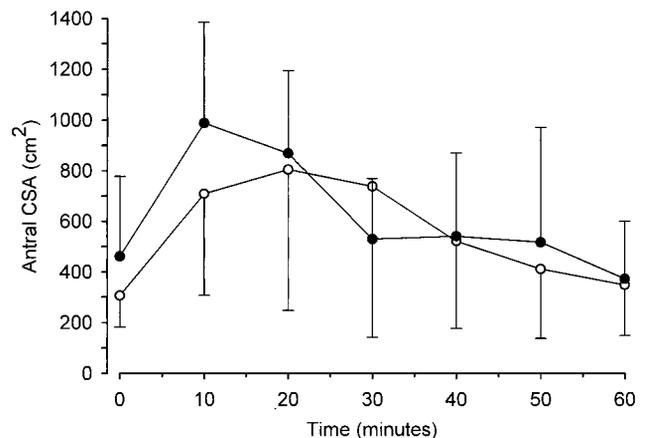
**Table 1. Subject Characteristics**

Age (yr)	$31 \pm 4$
Height (cm)	$164 \pm 5$
Prepregnancy weight (kg)	$62 \pm 10$
Term pregnancy weight (kg)*	$74 \pm 10$
Prepregnancy BMI	$23.1 \pm 3.7$
Gestation (weeks)*	$37.2 \pm 0.2$

(N = 11)

\* First study day. Data are mean  $\pm$  SD.

BMI = body mass index.



**Fig. 3.** Mean antral cross-sectional area (CSA)  $\pm$  SD (error bars) versus time for nine study subjects. Open circle = 50 ml water; filled circle = 300 ml water.

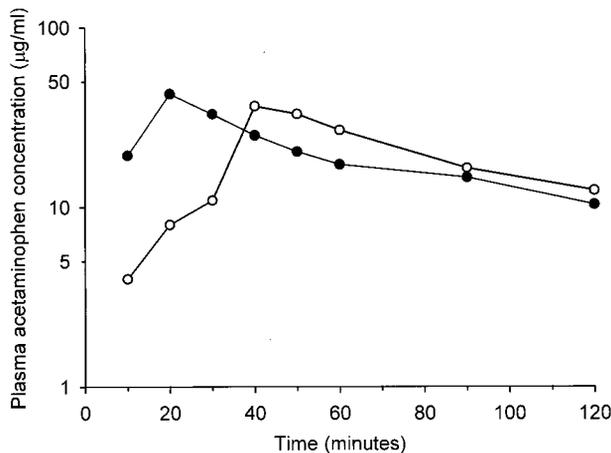


Fig. 4. Plasma acetaminophen concentration *versus* time relations for study subject no. 4. Open circle = 50 ml water; filled circle = 300 ml water.

## Discussion

Presurgical fasting guidelines serve to improve patient safety by minimizing the risk of aspiration but are balanced against the increased incidence of patient dehydration, hypoglycemia, dissatisfaction, hunger, and anxiety after prolonged fasting.<sup>8</sup> Presurgical fasting guidelines for clear liquids have been liberalized in the past decade,<sup>20</sup> as evidence accumulated that clear liquid ingestion up to 2 h before the induction of anesthesia does not result in larger gastric volumes compared with an overnight fast.<sup>1-7</sup> Although pregnant women are at increased risk for starvation-induced hypoglycemia and ketosis,<sup>21,22</sup> none of these studies included pregnant women.

The results of the current study support our hypothesis that gastric emptying in healthy, term, nonlaboring pregnant women after ingestion of water does not differ, or is faster than that observed in the same individuals after an overnight fast. Both T<sub>1/2</sub> and time to peak acetaminophen concentration decreased after ingestion of 300 ml water compared with 50 ml, and average gastric volume (as indirectly measured by antral CSA) was less than the average baseline value 60 min after ingestion of 300 ml water. This is consistent with the

observation of other investigators that gastric emptying may actually increase after a liquid meal.<sup>2,4,7</sup> The increase in the gastric emptying of 300 ml water may be because of the fact that gastric emptying of fluid volumes of 200 ml or more is an exponential function of stomach volume, whereas the emptying of small fluid volumes depends more on the phase of the gastrointestinal motility cycle during which it is consumed.<sup>23</sup> Inclusion of the ultrasound data from study subject no. 12 (had the 50-ml CSA been followed to CSA1/2) would not have altered this conclusion, as this would have prolonged the mean 50-ml CSA even more compared with the 300-ml CSA.

Our acetaminophen data are consistent with those reported by Macfie *et al.*<sup>10</sup> for fasting patients presenting for cesarean section. Other investigators have found that gastric emptying of a liquid meal in term pregnant women is not delayed compared with that in nonpregnant control subjects.<sup>9,11-13</sup> Therefore, it is not unexpected that the results of our study, comparing gastric emptying of pregnant women after ingestion of 300 ml water with that after an overnight fast, would be similar to results obtained in studies of nonpregnant patients.<sup>1-4</sup> Taken together, the results of these studies suggest that allowing pregnant patients to ingest clear liquids up to several hours before an elective surgical procedure would not result in increased gastric volumes at the time of induction of anesthesia. A larger study is indicated to determine whether liberalizing preoperative fasting guidelines for term pregnant women scheduled for elective surgery is safe.

Methods for measuring gastric emptying are limited during pregnancy. Scintigraphy is widely used in the nonpregnant population but requires exposure to radiation. Gastric aspiration is the best method for studying liquid meals<sup>24</sup> but requires the passage of an orogastric or nasogastric tube, a process unlikely to be well tolerated in an awake pregnant volunteer. The epigastric impedance technique has been described in pregnant women, but the stomach could not be located in one third of term pregnant women in one study<sup>12</sup> and its use is less well validated than other techniques.<sup>24</sup> Therefore, we elected to use ultrasound to measure actual gastric emptying and acetaminophen absorption as an indirect measure of gastric emptying.

Real-time ultrasonographic assessment of gastric emptying in term pregnancy was described by Carp *et al.*<sup>16</sup> Its use in measuring gastric emptying after a liquid meal has been validated in other study populations by comparison to scintigraphy,<sup>14,18,25</sup> including the assumption that a CSA of a single section of the gastric antrum is proportional to intragastric volume.<sup>14,18,26</sup>

Acetaminophen absorption is an indirect measure of gastric emptying. Acetaminophen is not absorbed in the stomach but is rapidly absorbed from the small intestine. Therefore, the rate of its appearance in the circulation is

Table 2. Plasma Acetaminophen Data

	50 mL	300 mL
AUC <sub>60</sub> (µg · min · ml <sup>-1</sup> )	1018 ± 397	1091 ± 306
AUC <sub>90</sub> (µg · min · ml <sup>-1</sup> )	1529 ± 502	1587 ± 424
AUC <sub>120</sub> (µg · min · ml <sup>-1</sup> )	1949 ± 606	1988 ± 520
AUC <sub>infinity</sub> (µg · min · ml <sup>-1</sup> )	4246 ± 1312	4474 ± 1511
C <sub>max</sub> (µg/ml)	32.9 ± 11.2	30.7 ± 13.0
t <sub>max</sub> (min)	40.9 ± 19.2	24.6 ± 12.1*

(N = 11) \* Different than 50 ml (P < 0.05).

AUC = area under the curve at 60, 90, and 120 min, and on extrapolation to infinity; C<sub>max</sub> = maximum plasma concentration; t<sub>max</sub> = time to maximum plasma concentration.

an indirect measure of gastric emptying. Its use in the measurement of gastric emptying of liquid meals has been validated by comparison with scintigraphy.<sup>15,27</sup> Acetaminophen absorption has been used frequently in studies of gastric emptying during pregnancy, although its use during pregnancy has not been validated.

The crossover design of the current study had several advantages. The increase in acetaminophen elimination clearance during pregnancy<sup>28</sup> makes comparison of results with nonpregnant controls problematic, but the crossover design of the current study controls for this variable. There is large intersubject variability in gastric emptying using various measurement techniques.<sup>18,26,29,30</sup> The crossover study design was necessary to control for this.<sup>23</sup> Intrasubject variability in the gastric emptying of semisolids and liquids is insignificant compared with intersubject variability.<sup>30</sup>

Body position and mobility affect gastric emptying. For example, compared with ambulation, lying on the left side was associated with delayed gastric emptying of liquids as measured by acetaminophen absorption.<sup>31</sup> We measured gastric emptying by ultrasound with the study subjects in the semiupright position, as described by Carp *et al.*<sup>16</sup> Our results may have been different (delayed gastric emptying) if the subjects had been in the lateral position. However, most ambulatory preoperative patients who drink before hospital admission are not recumbent, and this would therefore be unlikely to negatively influence gastric emptying in the preoperative period.

There is a general belief that preoperative anxiety may negatively influence gastric emptying. Subjects in the current study were not studied in the preoperative period. However, several small studies addressing this issue found no difference in gastric emptying in the preoperative compared with postoperative period,<sup>32-34</sup> even with documentation of increased anxiety in the preoperative period.<sup>34</sup>

Although liquids empty rapidly from the stomach, the rate of gastric emptying of caloric or acidic liquids is delayed compared with the rate of noncaloric liquids.<sup>35,36</sup> Nonetheless, recent guidelines do not differentiate among various clear liquids. In most studies of nonpregnant preoperative patients, the study group drank water or a nonsugared liquid. However, when patients were allowed to drink sugared liquids, their residual gastric volumes were no larger than that of the fasted patients.<sup>1,6,7,37</sup> Therefore, although the gastric emptying of caloric liquids is delayed compared with that of water, this delay is unlikely to be clinically significant.

We studied nonobese women. The data concerning gastric emptying in the obese population are contradictory. Using radiolabeled food-liquid assessment techniques, various studies have found that gastric emptying of solids and liquids is delayed, unchanged, or more

rapid in the obese compared with the lean population.<sup>38</sup> Clearly, our results cannot be assumed to apply to obese pregnant women.

Finally, the critical determinant of morbidity or mortality associated with pulmonary aspiration is gastric volume and pH.<sup>39</sup> We did not measure either. The clinically relevant question is whether term pregnant patients should be allowed to drink clear liquids up to several hours before elective surgical procedures, as is currently the standard of care for nonpregnant patients. The finding that gastric emptying after ingestion of water is not prolonged compared with that after an overnight fast does not directly answer this question. Theoretically, a patient could have a large gastric volume at the time of induction of anesthesia and be at risk for pulmonary aspiration despite having a fast gastric-emptying time.

In summary, we showed that gastric emptying in healthy, term, nonobese, nonlaboring pregnant women is not delayed after ingestion of 300 ml water compared with that after an overnight fast, and that gastric antrum CSA after ingestion of 300 ml water is, on average, less than that at baseline at 60 min. A larger study is indicated to determine whether it is safe to allow pregnant women to ingest clear liquids up to several hours before a planned surgical procedure, as is the current standard for nonpregnant patients.

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