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INFLUENCE OF AGE ON GALLBLADDER MORPHOMETRY

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ABSTRACT

Morphometric properties of the gallbladder such as length, diameter and volume are determinants of gallbladder function. These parameters are altered with age and may explain the age-related reduction in gallbladder contractility associated with gallstone formation. Ninety-two gallbladder specimens of subjects aged between 21 and 84 were sourced from City mortuary and the Department of Human anatomy during autopsy. For each gallbladder specimen, measurements of length and circumference were taken to the accuracy of 0.1millimetres (mm) and used to calculate the gallbladder volume. These measurements were standardized using measurements of liver length and weight. Data were recorded by age categories in age groups of 21-30, 31-40, 41-50, 51-60 and 61 or more years. The mean gallbladder volume was 47.948 (±19.080) cm^3 and showed a statistically significant increase with age ($p < 0.001$). There was also a significant increase of gallbladder length ($p = 0.01$) and diameter ($p < 0.001$). A positive correlation was observed between gallbladder length, diameter and volume; 0.282, 0.485 and 0.480 respectively ($p = 0.01$). The gallbladder volume which is a function of length and diameter, shows a statistically significant increase with age. Notably, there is a marked increase in these parameters after the fifth decade. This could explain the exponential increase in prevalence of cholelithiasis by 4 to 10 times after the fifth decade of life.

Keywords: Gallbladder volume, Contractility, Age, Cholelithiasis

INTRODUCTION

Gallbladder size and volume (GBV) are important determinants of gallbladder contraction and function. These parameters have been observed to increase with age (Palasciano, 1992). Individuals with a higher resting gall bladder volume have less post prandial fractional emptying and a higher residual volume after meals (Kishk et al., 1987). It is also established that large gallbladder volumes observed in older individuals are predictors of impaired gallbladder motility and bile stasis which predispose one to gall stone as well as biliary sludge formation (Murray et al., 1992; Caroli-Bosc et al., 1999). Other than in advanced age, the GBV also increases in physiological processes such as pregnancy (Van Bodegraven et al., 1998). As observed with increased age, the preponderance of gallstone formation is also increased in pregnancy.

Reduction in gallbladder contractility leads to biliary stasis and sludge formation hence the increased tendency of older individuals to form gallstones which result to cholecystitis (Caroli-Bosc et al., 1999). The prevalence of cholelithiasis has been reported to increase, with a marked escalation from 4 to 10 times higher after the fifth decade of life (Ogutu et al., 1990; Stinton and Shaffer, 2012). Age related changes in anatomical parameters such as gallbladder size and volume may explain the reduction of gallbladder contractility observed with age. This study therefore aims to describe the age-related changes in the morphometric properties of the gallbladder that may serve as the anatomical basis for the loss in gallbladder contractility with age and hence the high incidence of cholelithiasis in older individuals.

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MATERIALS AND METHODS

Ninety two gallbladders specimens of subjects aged between 21 and 84 were sourced from City mortuary and the Department of Human Anatomy, University of Nairobi. Ethical approval was sought from the Kenyatta National Hospital- University of Nairobi Ethics and Research Committee (KNH-UoN ERC) before commencement of the study. Specimen obtained from adult subjects aged ≥ 21 years were in used in the study. This was to ensure that the gallbladders studied did not exhibit growth changes as connective tissue growth stops at approximately 20 years of age (Schwartz et al., 2003).

Specimens from subjects with congenital anomalies of the biliary tree, cholelithiasis, pregnancy, obvious diffuse gallbladder wall thickening due to cholecystitis, trauma to the right hypochondriac region of the abdomen and evidence of previous surgical exploration and manipulation of the hepatobiliary system were excluded. The 92 subjects were included in this study and grouped based on age as shown in the table 1.

Accessing and examination of the liver and the gallbladder

At autopsy, a midline incision was made through the anterior abdominal wall from the xiphi-sternum to the pubic symphysis allowing access into the peritoneal cavity. An incision extending laterally from the midline along the 10th rib on the right side was also made to expose the entire length of the liver. The flaps were retracted laterally to expose the liver and the rest of the abdominal viscera. The hepatoduodenal ligament was located and severed as well as the common bile duct near the ampulla of Vater. The hepatic veins and the triangular ligaments were severed to free the liver from the inferior vena cava and the diaphragm respectively. Care was taken to avoid trauma to the gallbladder as the liver was being removed.

Measuring gallbladder and liver sizes

The gallbladder length was measured from the tip of the fundus to the beginning of the junction of the cystic duct and the Hartmanns pouch (figure 1) using a digital vernier calliper to the accuracy of 0.1mm. A string was wound around the internal surface of the gallbladder at the point of maximal width (figure 1) and the length measured using a digital vernier callipers to the accuracy of 0.1mm; this measurement represented the internal circumference of the gallbladder. This was used to calculate the diameter of the gallbladder using the formula: $C= \pi D$.

Where: C is the internal circumference in mm.

π is the constant pie 3.142

D is the internal diameter.

The maximal length of the liver was taken from the right lobe to the tip of the left lobe using a Haco® ruler to the accuracy of 1mm. The weight of the liver was measured in grams using an electronic weighing balance SF-400c and findings recorded on data sheets. These measurements were used to standardize morphometric measurements of the gallbladder. Specimens for histological processing measuring 0.5mm X 0.5 mm was obtained from the neck, body and fundus.

Table 1: Age of the subjects included in the study

Age group (years)	Number of subjects (n)
21-30	20
31-40	18
41-50	18
51-60	18
≥61	18

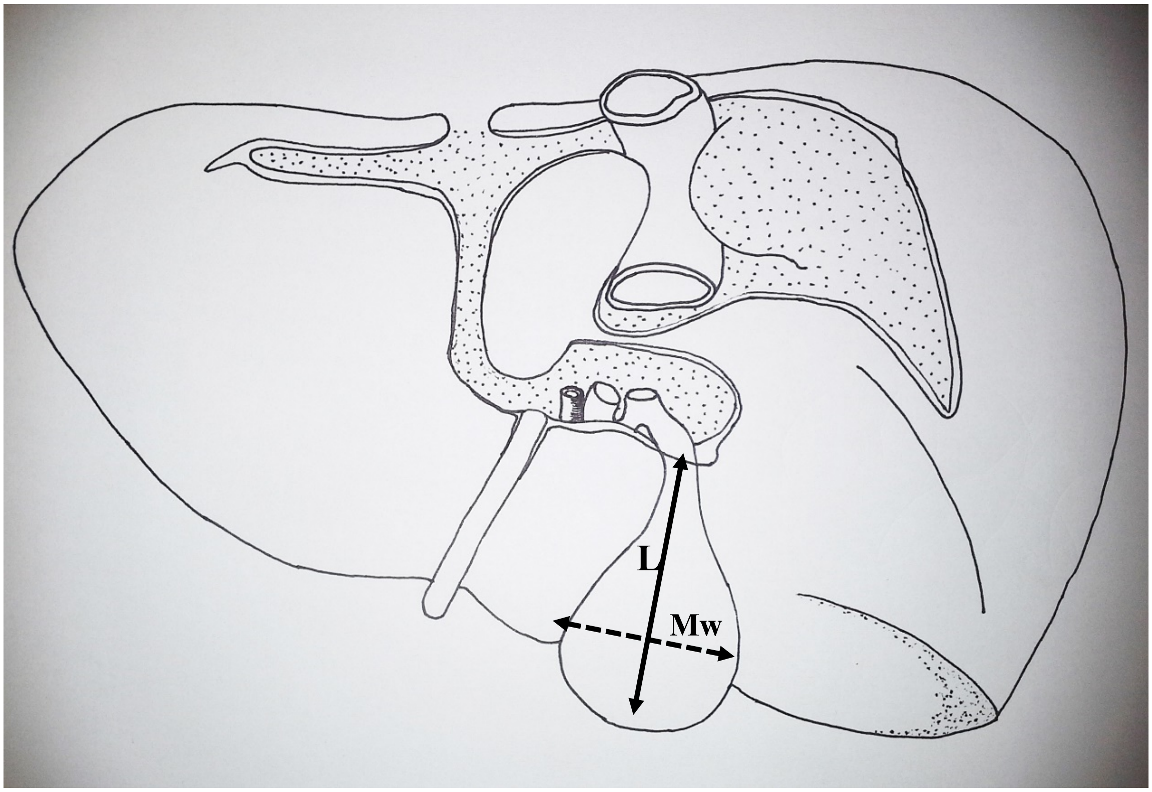

Figure 1: A schematic drawing showing the measurements used in estimating volume of the gallbladder. Gall bladder length (L) and maximum width (Mw) where the internal diameter was measured.

Calculation of gallbladder volume

The gallbladder volume was calculated using the ellipsoid formula described below (Dodds et al., 1985).

$$\frac{\pi}{6} \text{ x L x W x H}$$

Where:

π is the constant pie 3.142

L is the length of the gallbladder in mm

W is the width of the gallbladder in mm

H is the anteroposterior height of the gallbladder

The internal gallbladder diameter obtained was be taken to be equal to the maximal width as well as the anteroposterior height. Hence the formula was adjusted to:

$$\frac{\pi}{6} \text{ x L x } \mathrm{D}^2$$

Where:

п is the constant pie 3.142

L is the length of the gallbladder in mm

D is the internal diameter.

Since the gallbladder size and hence volume maybe affected by body size, this measurement was standardized using the liver length and weight.

Data management and statistical analysis

Morphometric data depicting gallbladder length and volume were entered into SPSS software (Version 21.0, IBM) for statistical analysis. Means and standard deviations for morphometric measurements were calculated and were standardized and adjusted for liver weight and length. Assuming a normal distribution curve, oneway ANOVA, Kruskal Wallis and Mann-Whitney U tests were used to determine statistical significance between the morphometric variables in different age groups. Pearson's correlation coefficient was used to determine the association between the gallbladder length, diameter and volume with age. In both instances, a p-value of <0.05 was considered significant at 95% confidence interval. Tables and charts were used for data presentation.

RESULTS

The ages of the subjects included ranged from 21 - 84 years (mean 40.08 ±17.985).

Age related changes in the gallbladder length

The length of the gallbladder ranged from 56 – 141 mm with a mean of 97.35 ±15.537 and median of 98 mm. It increased in length from 96.9 mm in the 3rd decade to 106.3 mm in the 7th decade and beyond. A marked increase from 97.7 mm to 102.9 mm was observed between the 31 – 40 and the 41 – 50 age groups (Table 2) [Figure 2a].

Age related changes in the gallbladder diameter

The diameter of the gallbladder ranged from 25 – 37 mm with a mean of 30.035 ±5.552 and a median of 31 mm. An increase from 28.1 mm in the 3rd decade was noted to 34.1 mm in the 7th decade and beyond. (Table 2) A relatively larger increase was noted between 31 – 40 and the 41 – 50 age groups compared to the rest (32. 2 to 26.7 mm) [Figure 2b].

Age related changes in the gallbladder volume

The GBV ranged from 34.184 – 74.227 cm^3 with a mean of 47.948 ±19.080 cm^3 and a median of 48.6 mm. There was a similar pattern of increase as observed in gallbladder length and diameter where the difference between the 4th and 5th decades appeared to be greatest (44997.8 to 55887.0 mm^3) while the increase from the 3rd decade to 7th decade and beyond was 40123.4 to 64550.3 mm^3 [Figure 2c].

Using ANOVA the differences between the means was found to be statistically significant. A post hoc analysis using Scheffé's test revealed that this was due to the significant difference in the mean gallbladder length in age group 21 - 30 years and age groups 41 – 50 and 51 – 60 years. The significant difference in the mean gallbladder diameter as well as mean gallbladder volume was due significant differences between age group 21 - 30 years and age groups 41-50, 51-60 and ≥ 61 years.

Table 2: Age related changes of the gallbladder length, diameter and volume.

Age group (years)	**Mean gallbladder length (mm)**	**Mean gallbladder diameter (mm)**	**Mean gallbladder volume (mm^3)**
21-30	96.91±19.58	28.12±6.36	40123.41±11119.65
31-40	97.69±12.84	29.66±4.81	44997.77±15646.41
41-50	102.88±8.12	32.21±2.71	55887.03±11217.20
51-60	104.53±8.94	33.46±3.65	61276.15±14948.08
≥61	106.27±13.91	34.06±3.81	64550.35±16946.35
P-values	0.01	<0.001	<0.001

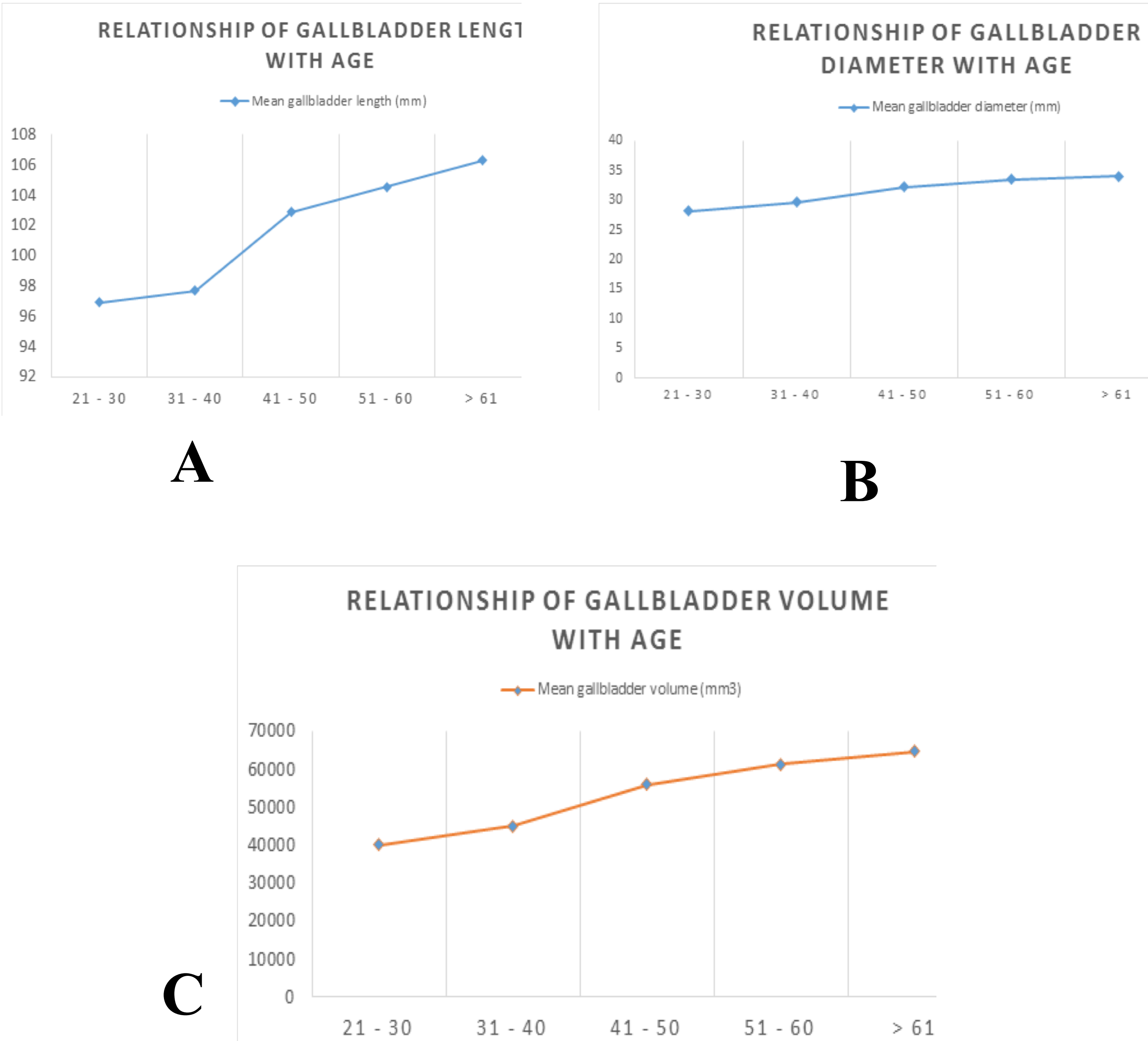

Figure 2: Line graph showing the relationship between Age in years and **[A]** mean gallbladder length in mm, **[B]** mean gallbladder diameter in mm, **[C]** mean gallbladder volume in mm^3.

DISCUSSION

Gallbladder contractility decreases with age resulting in biliary stasis which predisposes to gallstone formation (Caroli-Bosc et al., 1999). Changes in the gallbladder size and volume may contribute to the loss in function observed. Salient age-related changes described in the present study include: an age-related increase in length, diameter and volume of the gallbladder with a marked increase between the fourth and the fifth decade.

In the current study, it was observed that on average the gallbladder length ranged from 5 – 14 cm. These findings are comparable to reports by Rajguru et al., (2012), Pirraci et al., (2013) and Prakash et al., (2013) who reported the average length to range from 5 -12 cm. In contrast to these reports, findings from the current study suggest a wider range of values in the study population. The wide range observed in the current study may be because the gallbladder specimens used in the current study were obtained from older cadaveric specimen since increase in gallbladder size is observed with age (Palasciano, 1992). Despite significant differences in the sample sizes, methodologies employed as well as possibility of existing ethnic and population variations, the results obtained from various studies appeared to be in tandem. Prakash et al., (2013) carried out a cadaveric study in an Indian population recruiting a sample of ninety specimen while Rajguru et al., (2012) recruited sixty cadaveric specimen from the same population and obtained similar results (table 3). Pirraci et al., (2013) who studied 9481 subjects from an Albanian population taking measurements by ultrasonography also obtained similar results. These findings further suggest that measurements obtained from cadaveric specimen and those from ultrasonography done *in vivo* are comparable.

The current study also reports an age-related increase in gallbladder length. A similar observation was made by Palasciano et al., (1992) suggesting an age-related increase in gallbladder size. In the current study, the pattern of increase was such that a gradual increase was noted between all the age-groups. Notably, the greatest degree of increase was observed between the 31 – 40 years and 41 – 50 years suggesting a significant change in the gallbladder structure due to distention after the fifth decade. This is in agreement with reports of marked escalation of prevalence of cholelithiasis by 4 to 10 times after the fifth decade of life (Ogutu et al., 1990; Stinton and Shaffer, 2012). However, the general pattern of increase observed in the current study differs with that reported by Adeyekun and Ukadike, (2013) who observed that the length of the gallbladder in Nigerian population increased all through the age groups and showed a slight after the between 61 – 70 years and 71 – 80 years age groups. This decline which is not observed in our study may be due to the difference in age stratification where the current study grouped all subjects above 60 years old together while Adeyekun and Ukadike, (2013) further stratified their sample such that those above 60 years were grouped in their respective decades. However, gallbladder parameters in the elderly and in centenarians show minimal differences and hence age-related changes in after the seventh decade are not significant (Romano et al., 2004).

The gallbladder diameter reported in the current study ranged from 25 – 37 mm. Nadeem, (2016) reported that the gallbladder width in a sample Indian population obtained from gross measurement of cadaveric specimen ranged from 27 – 52 mm. Rajguru et al., (2015) also obtained comparable findings estimating the gallbladder width in the same population to be approximately 25 – 50 mm. Similarly, Piracci et al., (2013) carried out a study on a sample Albanian population using ultrasonography to obtain a width of 25 – 50 mm. From the above comparisons, it is clear that the gallbladder widths in different populations and obtained by different modalities are comparable. This is despite the current study obtaining a narrow range possibly because the internal diameter was measured as opposed to the external width which was the measurement of choice in other studies. In addition, the comparison demonstrates that measurements obtained from cadaveric studies can be used to provide baseline data to be used by radiologists when interpreting ultrasonographic images of the gallbladder.

Table 3: Comparison of gallbladder length in different populations.

Reference	Population	Sample size (n)	Method	Length (cm)
Nadeem, 2016	Indian	100	Cadaveric	4.5 – 11.6
Rajguru et al., 2012	Indian	60	Cadaveric	5 – 12
Pirraci et al., 2013	Albanian	9481	Ultrasonography	5 - 12
Prakash et al., 2013	Indian	90	Cadaveric	7 - 10
Desai and Bhojak, 2015	Indian	50	Cadaveric	4.5 - 11
Current study	Kenyan	92	Cadaveric	5 - 14

The gallbladder diameter also exhibited a similar pattern of increase suggesting an increase in width with age which is comparable to the increase in gallbladder length.

In the current study the gallbladder volume (GBV) on average was 48 (±19) cm^3. These findings differ greatly with reports from other workers. Ugwu and Agwu, (2010) and Adeyekun and Ukadike, (2013) reported that gallbladder volumes in a Nigerian population were 27 ±13 cm^3 and 29 ± 14 cm^3. Similarly, studies on Turkish and American normal subjects report an average GBV of 28 ± 12 cm^3(Kishk et al., 1987; Sari et al., 2003). The high values obtained from the study may be due to the differences in methodology employed. Previous studies used measurements obtained from ultrasonography to calculate the GBV. The current study, however, obtained measurements from cadaveric specimen which may be less accurate due to alteration of tissue structure after death. In addition, the difference may because the current study assessed age changes in adults (above 21 years) while the other studies took measurements from subjects below 18 years which may have exhibited growth changes rather than age changes. Majority of the specimens used for calculation of gallbladder volume in the current study were obtained from subjects above the age of 40 with approximately one fifth being more than 60 years old. The use of specimens obtained from older individuals in the current may account for the greater volumes observed since GBV increases with age (Caroli-Bosc et al., 1999; Yoo et al., 2003).

Concordant to reports by Caroli-Bosc et al., (1999) and Yoo et al., (2003) the current study reports a significant increase in GBV with age as well as a positive correlation between the two variables. An increase in resting GBV is also observed in physiological conditions such as pregnancy where it has been noted to increase two-fold after the first trimester (Braverman et al., 1980). The increase in GBV is due to a reduction in motility caused by progesterone which limits G protein actions, thus impairing contractions (Van Erpecum et al., 2000). GBV also increases in diabetes type II. This is caused by a reduction in motility due to autonomic neuropathy (Kishk et al., 1987; Agarwal et al., 2004). As observed in pregnancy and diabetes type II, an age-related increase in GBV is due to reduced gallbladder motility evidenced by a reduction in the gallbladder contraction index (GBCI) [Caroli-Bosc et al., 1999; Ugwu and Agwu, 2010]. Consequently, large GBVs are predictors of hypomotility and hence increase the risk of gall stone formation (Murray et al., 1992).

In conclusion, the gallbladder volume which is a function of length and diameter increases with age. Notably, there is a marked increase in these parameters after the fifth decade. This could explain the exponential increase in prevalence of cholelithiasis by 4 to 10 times after the fifth decade of life.

Limitations of the study

As this was a comparative study, it was necessary to match all parameters in the various subjects. These parameters include height, weight, nutrition status and lifestyle. However, these confounders could not be standardized since the information was not readily available.

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