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Sonographic measurement of the thymus in infants

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Abstract. A new method of measuring the size of the thymus in infants less than 1 year of age is presented. The width of the thymus was measured in a transverse image while the area of the largest lobe was assessed in a longitudinal image. The thymic index was then defined as the product of these two values. Intra- and interobserver variation analysis were performed in 23 infants. Each infant was scanned alternately by both of two radiologists, and later the same day the measurements were repeated. The mean differences between the first and second measurements (intraobserver variation) were −0.25 (2 SD 7.56) and −1.13 (2 SD 10.80), respectively, for the two observers. The mean difference between the first measurements of the two observers (interobserver variation) was 1.47 (2 SD 9.39). In a postmortem study of 12 infants the thymic index measured by sonography showed an acceptable correlation to the actual volume (c = 0.80) and weight (c = 0.87) of the thymus. In conclusion, our sonographic estimate of the volume of the thymus, the thymic index, in infants under 8 months of age seems to be easy, reliable and reproducible.

Key words: Thymus gland – Ultrasonography – Infant

Introduction

The thymus is the central organ for the differentiation of T-cell lymphocytes. The T-cells play a major role in the human immune system, and the size of the thymus demonstrates great variability between individual infants, and in the same infant at different times [1, 2]. The thymus diminishes in size in seriously malnourished infants, which suggests that there may be a relation between the size of the thymus and the status of the cellular immune defence of the infant [3, 4]. Some reports on the sonographic appearance of the thymus in infants and small children have been published [4–8], but with different techniques. In studies of the size of the thymus [4, 7, 8] no assessment of reproducibility has been offered. Neither has a comparison between sonographic findings and autopsy been made. The purpose of this study was to test a new sonographic method of estimating the size of the thymus in infants less than 1 year old. The study includes inter- and intraobserver analysis and a postmortem correlation of the sonographic measurements to autopsy results.

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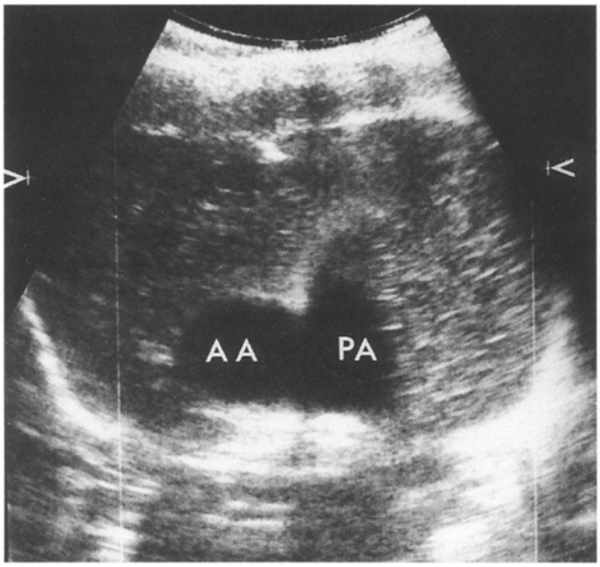
Materials and methods

After informed consent had been obtained from the parents, 23 infants (12 males and 11 females) entered the study. The median age of the infants was 4 days (range 1–255 days) and the median weight was 3800 g (range 1300–7600 g). Three infants had been born prematurely.

The study was approved by the Research Ethics Committee for Copenhagen and Frederiksberg City.

Sonography was performed with a sonographic scanner type 1846 (B & K Medical, Gentofte, Denmark) and a 7-MHz probe-type 8534 (sector 112°), or a B & K sonographic scanner type 3535 and a 7.5-MHz probe-type 8545 (sector 60°). At sonography the thymus appeared as a well-delineated echo-poor structure in the anterior mediastinum with an echostructure similar to that of the liver. Using a transsternal approach, the largest transverse diameter (width) of the thymus was obtained (Fig. 1). Next, in longitudinal images the area of the largest lobe was assessed (Fig. 2). Both measurements were taken using the built-in calliper of the scanner. The two measurements were multiplied and defined as the thymic index, which represented a sonographic estimate of the thymic volume. Each infant was scanned with hidden calliper readings, alternately by both radiologists (H. H. and M. B. N.), while the other was outside the room. Later the same day the measurements were repeated.

1 

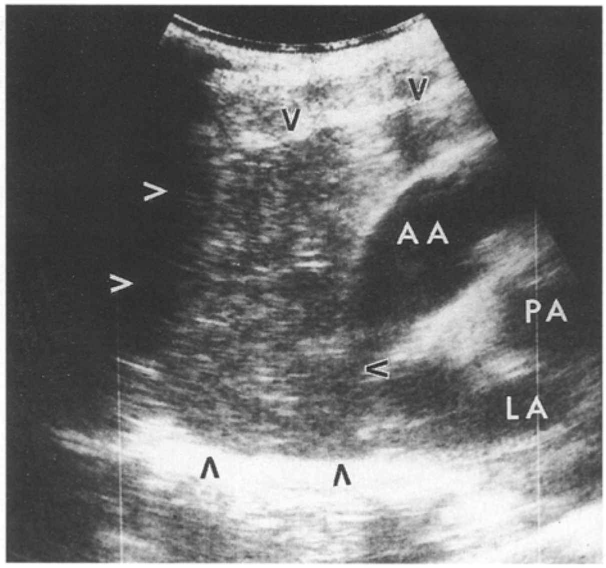
 2

Fig. 1. Transverse sonogram of the thymus obtained by transsternal scanning in a 4-month-old child. The thymus is in the anterior mediastinum in front of the large vessels and has a homogeneous echo-poor structure. Transverse diameter of the thymus is measured between *arrowheads*. *PA* pulmonary artery; *AA* ascending aorta

Fig. 2. Longitudinal sonogram of the thymus *(arrows)* allows a sagittal area to be measured. *PA* pulmonary artery; *AA* ascending aorta; *LA* left atrium

Reproducibility was analyzed according to Bland and Altman [9]. Intraobserver variation was calculated by using the first and second measurements of the same observer. The interobserver variation was calculated by comparing the first measurements of the two examiners.

In 12 deceased infants the size of the thymus was measured by sonography as described above just before autopsy. The cause of death was crib death (6), pneumonia (2), extreme prematurity (1), sepsis (1), congenital heart disease (1) and 1 infant was stillborn. At autopsy the pathologist determined the transverse diameter and the weight of the thymus, and the thymus was submerged into water to estimate the volume. The pathologist was without knowledge of the sonographic findings. For statistical analysis Pearson's correlation and linear regression were used.

Results

Figures 1 and 2 illustrate the sonographic appearance of the thymus and the method of measurement used. Figure 3 a and b shows the intraobserver variation for sonographic measurements of thymic index. The mean differences between the first and second measurements were –0.25 (2 SD 7.56) and –1.13 (2 SD 10.80), respectively, for the two observers. Figure 3 c shows the interobserver variation. The mean difference between the first measurements of the two observers was 1.47 (2 SD 9.39).

The correlation between the sonographic measurement and the autopsy results for 10 children is shown in Table 1. Another 2 infants were examined, but are not included in the table: in 1 infant because of the extreme size of the thymus (transverse diameter 11 cm), which extended beyond the image sector of the transducer, and in 1 infant because it was not possible to distinguish the thymus from the lungs. (The infant was stillborn and had not breathed). No abnormalities involving the echostructure of the thymus were observed, but the time interval from death to sonography influenced the quality of the US picture, which decreased. The pathologist measured the transverse diameter of the thymus before it was removed from the thorax in 2 infants (no 1 and 3 in Table 1), and after it had been removed in the remaining 8 infants. There was a good agreement between sonographic width of the thymus and the width at autopsy ($c = 0.93$, $R^2 = 0.87$, $p = 0.0001$). The agreement between the thymic index and the actual weight ($c = 0.87$, $R^2 = 0.77$, $p = 0.0009$) and volume ($c = 0.80$, $R^2 = 0.65$, $p = 0.02$) was less precise, but acceptable. The linear correlation between the thymic index and the actual volume is illustrated in Fig. 4.

Discussion

The thymus, which provides the environment for T-cell differentiation in small children, may diminish in size in seriously malnourished infants [1, 3, 4]. Previous studies [4–8] have shown that sonography can be used for imaging of the thymus in infants, and in contrast to CT, sonography requires no patient sedation and involves no ionizing radiation [10, 11]. Thus far only three reports have described sonographic measurements of the size of the thymus: one in healthy infants aged 2–8 years [7], one in seriously malnourished infants aged 6–55 months [4] and one in healthy infants under 1 year [8]. The first two studies used the anteroposterior thickness and the length of the thymus from measurements obtained in a sagittal scanplane [4, 7]. The last study measured the anteroposterior diameter of both lobes, the transverse diameter and the craniocaudal extent of

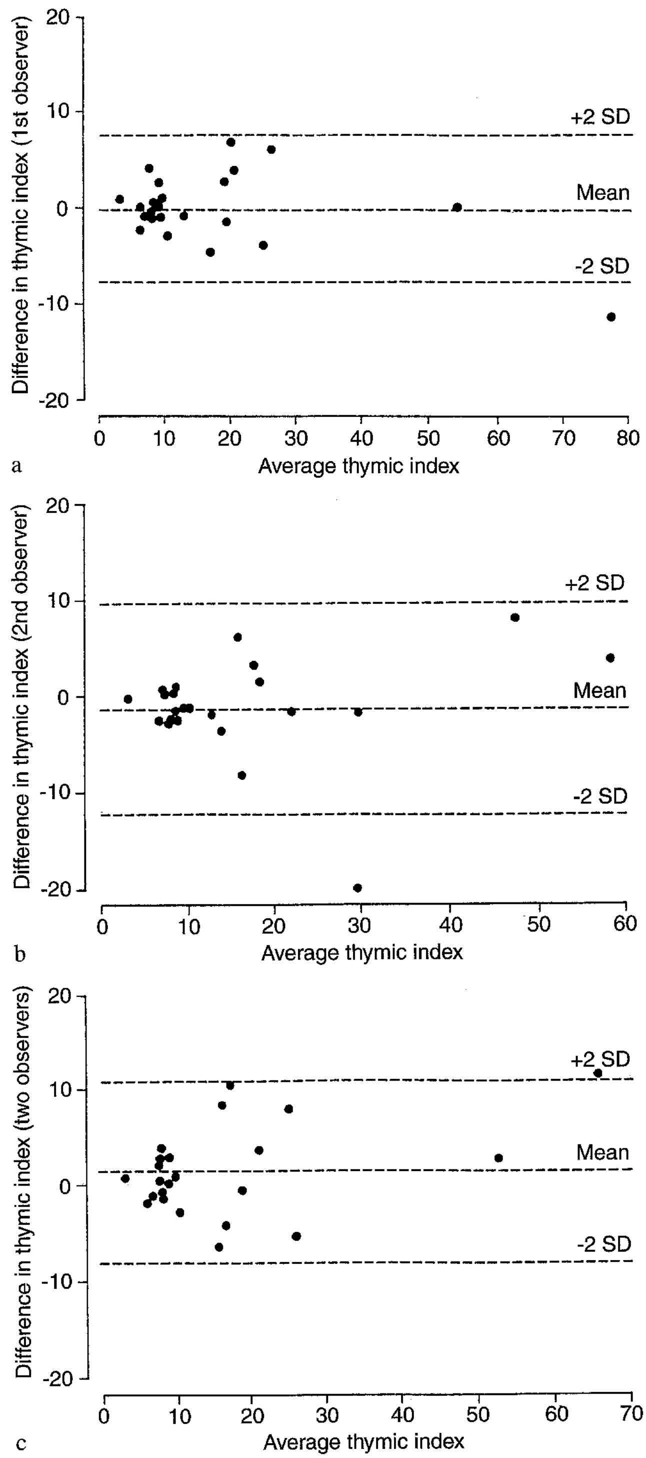


Fig. 3 a–c. Reproducibility (Bland and Altman plots) of the sonographic measurement of the thymic index. **a, b** Intraobserver variation for the two examiners. **c** Interobserver variation between the two examiners

the thymus [8]. None of the studies, however, assessed the volume of the thymus. Theoretically, the volume would be the most correct way of describing the size of the thymus. In this study we wanted to establish an easy and reliable method for assessing the size of the thymus in infants less than 1 year old, the period of life in which the thymus is probably of greatest importance [1].

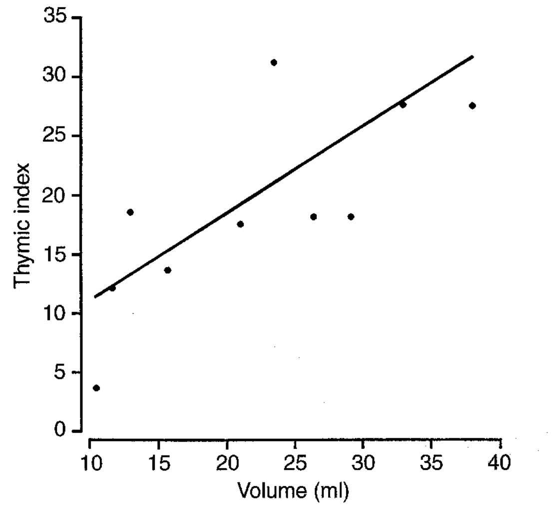


Fig. 4. The linear correlation between the thymic index and the volume measured at autopsy

In longitudinal images we measured the sagittal area of the thymus instead of the length and thickness, which has been used by others [4, 7, 8]. We chose this method (Fig. 2) in order to minimize the influence of respiration on the measurements, especially in the sagittal plane, where the thymus shows a tendency to flatten during heavy respiration, and also because we think that the craniocaudal length measurement may be unsuitable as part of a volume estimate, because the most caudal extent of the gland anterior to the heart will only add very little to the volume of the gland.

Because the thymus, consisting of two lobes, fills in the spaces between the great vessels and the anterior chest wall as if moulded by these structures, the shape of the thymus may be affected by both the respiration and the heartbeat. A detailed assessment of thymic size would therefore include assessing the two lobes and the intermediate section of the gland in the same stage of respiration and in the same phase of the cardiac cycle. This would be very time-consuming and therefore not suitable for clinical situations. The sonographic measurements described in this study give only a gross estimate of the thymic volume, but with some practice the examination is easy to perform and takes only a few minutes.

In order to correlate our thymus index to the precise weight and volume, deceased infants were scanned immediately before autopsy. The transverse sonographic measurement corresponded well with the result from the autopsy, but the correlation between the thymus index and the true volume and weight was poorer, but more informative in clinical situations. Theoretically, the sonographic thymic index should indicate a larger volume than the true volume, especially if there was a pronounced asymmetry of the two lobes. This was not the case, and because the transverse dimensions showed a good correlation, the maximum sagittal area must have been underestimated. A more precise volume determination might be obtained by using a planimetric method [12], but that would require special US equip-

Table 1. Sonographic measurements of thymic size in 10 deceased infants compared with postmortem findings. One infant had been born prematurely

Infant no.	Sonographic findings		Postmortem findings			Weight of infant (g)
	Width (cm)	Index	Width (cm)	Volume (ml)	Weight (g)	
1	1.1	0.4	0.9	–	0.25	482
2	2.3	3.7	3.3	10.5	10.9	2700
3	2.9	4.1	3.1	–	10.0	2700
4	3.5	13.7	4.0	15.7	16.2	4000
5	3.8	12.2	5.5	11.7	12.3	4000
6	3.8	18.6	4.1	13.0	13.6	3800
7	4.1	27.5	5.5	38.0	39.4	4200
8	4.3	17.6	5.0	21.0	21.6	7000
9	5.2	31.2	5.9	23.5	24.4	4200
10	5.3	27.6	5.5	33.0	34.8	4670

ment and cannot be used in clinical situations because the child would have to be anaesthetized. On the other hand, the problem is of less importance if the measurement is performed either as a follow-up study of the same infant or for classifying the size of the thymus in a given infant as either small, medium or large [3].

In conclusion, our sonographic estimate of the volume of the thymus, the thymic index, seems to be reliable and reproducible. The method may be used for assessing the growth of the thymus by repeated measurements or for comparing the thymic size in groups of children with diseases that affect the thymus, a subject that is currently under investigation.

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Erratum

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Due to an unfortunate error the name and address of the last author of the article "Two-dimensional coronary MRA: limitations and artefacts" by A. J. Duerinckx et al., published in vol. 6, issue no. 3, on pp. 312–325 was given incorrectly. We regret this error and herewith provide the correct name and address.

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