DOI 10.26724/2079-8334-2020-4-74-205-209
UDC 611.37.018:611.068]-053.15-053.31

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ANATOMIC VARIABILITY OF THE PANCREAS ORGANOMETRIC TRANSFORMATIONS IN HUMAN FETUSES AND NEWBORNS

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Pancreas studies were performed on 72 samples of human fetal corpses (from 4 to 10 months) with the mean parieto-calcaneal length of 165.0 to 500.0 mm and on 9 samples of newborns by means of morphological examination. It is established that in fetal and early neonatal ontogenetic periods the typical pancreas shape is curved (72±5 %) and its alternative forms are arched (18±4 %) and straight (10±2 %). The organometric pancreatic parameters and its anatomic parts have two periods of the accelerated development and one period of the relatively slow development. The second period of the relatively slow development is defined only for the gland body width. The model of predicting the standard values of pancreatic morphometric parameters has the following design: pancreatic length = β_0 + 0.094 x parieto-calcaneal length of a human fetal corpse, where β_0: 3.342 if the age period = 4 months; 4.731 = 5 months; 6.924 = 6 months; 10.349 = 7 months; 8.244 = 8 months; 13.821 = 9 months; 17.489 = 10 months; 18.087 = newborns.

Key words: pancreas, anatomy, fetus, newborn, human.

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АНАТОМІЧНА МІНЛИВІСТЬ ОРГАНОМЕТРИЧНИХ ПЕРЕТВОРЕНЬ ПІДШЛУНКОВОЇ ЗАЛОЗИ У ПЛОДІВ І НОВОНАРОДЖЕНИХ ЛЮДИНИ

Дослідження підшлункової залози виконані на 72 препаратах трупів плодів (від 4 до 10 місяців) від 165,0 мм до 500,0 мм тім'яно-п'яткової довжини та 9 новонароджених за допомогою морфологічних досліджень. Встановлено, що у фетальному та ранньому неонатальному періодах онтогенезу типовою формою підшлункової залози є зігнута (72±5 %), варіантні її форми – дугоподібна (18±4 %) та пряма (10±2 %). Для органометричних параметрів підшлункової залози та її анатомічних частин притаманно два періоди прискореного розвитку та період відносно сповільненого розвитку. Тільки для ширини тіла залози визначається другий період відносно сповільненого розвитку. Модель прогнозування нормативних значень морфометричних параметрів довжини підшлункової залози має вигляд: довжина підшлункової залози = β_0 + 0,094 х тім'яно-п'яткова довжина плода, де β_0: 3,342, якщо віковий період = 4 міс; 4,731 = 5 міс; 6,924 = 6 міс; 10,349 = 7 міс; 8,244 = 8 міс; 13,821 = 9 міс; 17,489 = 10 міс; 18,087 = Новонароджені.

Ключові слова: підшлункова залоза, анатомія, плід, новонароджений, людина.

The work is a fragment of the research project "Regularities of sex-age structure and topographic anatomical transformations of organs and structures of the body at the pre- and postnatal stages of ontogenesis. Features of perinatal anatomy and embryotopography", state registration No. 0120U101571.

Today, at the present stage of the society development, there is a paradoxical statement, namely, that the level and capabilities of modern diagnostic and preventive medicine are ahead of knowledge on the human body's normal structure. Many clinicians have come to the conclusion that it is impossible to justify the advisability of rational treatment methods without understanding the patterns of human body's development and structure. Therefore, morphological data are used to diagnose many diseases. Therefore, the study of individual human development patterns is an urgent problem of today [1, 2, 8, 11].

In recent years, there has been a significantly increased interest in clinical and variant anatomy due to the increasing use of diagnostic imaging methods (computed tomography and magnetic resonance imaging), which permit intravital determination of the body's organs and structures status. Many questions on the normal morphology and structures of the body are subject to revision, new handbooks of anatomical charts in classical and clinical anatomy are developed. Studies of individual anatomical variability patterns are connected with this topical field of the current morphology [3, 7, 10].

There is a well known description of the pancreatic gland (PG) as an organ that provides adequate digestion, external and internal secretion, and is involved in many physiological processes, from digestion up to adaptation processes, including maintaining homeostasis throughout the body [5].

The pancreas performs two main functions, depending on which its exo- and endocrine parts are distinguished. The function of the organ's exocrine part is to produce pancreatic fluid. The endocrine part of the pancreas is represented by small cell clusters - pancreatic islets, which are also called islets of Langerhans. Pancreatic islets consist of endocrine cells - insulocytes, between which the fenestrated type hemocapillaries pass, surrounded by pericapillary spaces [4, 9].

Anatomical studies of the pancreas in fetuses and newborns will permit to determine the morphological aspects of individual variability, which will serve as a basis for establishing different variants of structure and malformations in the postnatal period of ontogenesis, and can be used in the development of new surgical approaches and techniques in newborns and infants. The obtained new scientifically substantiated data on the organometric characteristics of the pancreas in fetuses and newborns are important for establishing criteria for the gland's development and its compliance with the terms of pregnancy [3, 6].

The purpose of the work was to clarify the features of the pancreatic gland's structure and topography and to establish its organometric parameters in human fetuses and newborns.

Materials and methods. Study of the pancreas ontogenetic transformations was performed on 72 samples of fetal corpses (from 4 to 10 months) with 165.0 to 500.0 mm of parieto- calcaneal length (PCL) and on 9 newborns of both sexes who died of causes not related to the digestive system diseases and without external signs of anatomical deviations or abnormalities and without obvious macroscopic abnormalities from the normal structure of the abdominal organs. Adequate anatomical methods were used during the study: macropreparation, magnetic resonance imaging, radiography, topographic anatomical sections and morphometry. Statistical analysis of the obtained data was performed using a licensed RStudio software. The null hypothesis that the samples were taken from a single distribution, or from distributions with the same medians, was tested:

H_0: { each group has identical distribution }

H_1: { each group does not have identical distribution }.

We used the Student's test, the nonparametric Kruskal-Wallis test to answer the question of whether there is a difference between the groups' distributions, but the above test does not specify which particular groups differ; the Conover-Iman test to compare stochastic dominance and to obtain results between different pairwise comparisons after the Kruskal-Wallis test for stochastic dominance among K groups.

When analyzing the sample correlation coefficient (r), the correlation strength was assessed by the Chaddock scale: at r = 0 – no correlation; at r = 0.1 – 0.3 – weak correlation; 0.3 – 0.5 – moderate strength correlation; 0.5 – 0.7 – noticeable correlation; 0.7-0.9 – high strength correlation, 0.9-1 – very high strength correlation. The values at $p < 0.05$ were considered statistically significant.

The work was performed in compliance with the basic provisions of the ICH GCP (1996), the Council of Europe Conventions on Human Rights and Biomedicine (dated 04.04.1997), the Helsinki Declaration of the World Medical Association on the ethical principles of scientific medical research with human participation (1964-2013) and the order of the MOH of Ukraine No. 690 dated 23.09.2009.

Results of the study and their discussion. Based on the pronouncement and direction of the pancreas anatomical parts, we have identified three main forms: curved, arched, straight. The typical form of PG in fetuses and newborns is curved, which is observed in 72±5% of cases, less often – arched (18±4%), rarely - straight (10±2%). Interestingly, the values of the mean percentages in the incidence of curved and straight forms of the pancreas are higher in 6-7-month-old fetuses, and lower – in early and late fetuses and newborns. In our opinion, this is due to the fact that in this age group, 8% of observations revealed variants of the pancreas structure. Curved and arched shapes of the gland are characterized by a larger head of the body. The pancreas head in all its forms is located ventrally and caudally to the body and tail.

To more accurately characterize the curved shape of the pancreas as a typical shape for the fetal and early neonatal periods of ontogenesis, we have substantiated the organ's characterization based on the correlations between the length of the gland and its anatomical parts. Reliably ($p < 0.05$) larger values of the pancreas head, body and tail lengths sum, compared to the length of the organ, generally ensure the accuracy (100%) of its curved shape study.

Given the pronouncement of the pancreas anterior border, we have identified two types of its cross section: flat and triangular. The flat type is typical of fetuses and newborns, but it decreases with fetal growth (in early fetuses it is detected in 78% of cases, in 6-7-month-old fetuses – 62%, in 8–10-month-old and newborns – 58%). In contrast, with the growth of fetuses, the number of triangular type of pancreas increases (in early fetuses – 22%, in late fetuses and newborns – 42%). It should be noted that the triangular type of the gland tail's cross-section reaches 55% of observations in late fetuses and newborns.

The pancreas is usually located retroperitoneally, only in 16% of cases in late fetuses and newborns it is located mesoperitoneally. In the triangular type, the tail of the gland is covered with peritoneum mesoperitoneally.

During the fetal and early neonatal periods of ontogenesis, the pancreas length increases from 14.41±0.28 mm (4-month-old fetuses) to 29.08±0.28 mm (neonatal period) (table 1). Organometric parameters of the pancreas length increase the most from the 4th to the 6th month and from the 7th month of fetal development to the neonatal period. Given the fact that from the 6th to the 7th month of fetal

development, the organometric parameters of the pancreas length increase slightly, this period can be called a period of delayed development.

According to the Conover-Iman test for pancreas length, the median difference for all possible age pairs is statistically significant, except for pairs "8 months – 9 months", "8 months – 10 months", "9 months – 10 months" and "10 months – Newborns ".

Table 1

Length of the pancreas in human fetuses and newborns (mm)

	Length of the pancreas	
	M±m	Confidence intervals limits
4 months	14.41±0.28	13.80-15.02
5 months	16.91±0.30	16.27-17.55
6 months	19.29±0.40	18.43-20.15
7 months	20.58±1.20	17.94-23.22
8 months	26.50±0.28	25.85-27.15
9 months	26.74±0.28	25.96-27.52
10 months	27.60±0.41	26.45-28.75
Newborns	29.08±0.28	28.43-29.73

The length of the pancreas head in fetuses and newborns increases from 7.02±0.16 mm (4-month-old fetuses) to 14.36±0.17 mm (neonatal period), while its width – from 4.10±0.16 mm up to 8.03±0.08 mm, respectively (table 2). Two periods of accelerated development of the pancreas head length from the 4th to the 6th month and from the 7th month of intrauterine development to the period of the newborn, and its width – from the 4th to the 5th month and from the 6th month of intrauterine development to the neonatal period.

From the 6th to the 7th month for the pancreas head length and from the 5th to the 6th month of intrauterine development for its width are referred to the period of relatively slow development. According to the results of the Conover-Iman test for the length and width of the pancreas head, the median difference for all possible age pairs is statistically significant, except for its length pairs – "5 months - 7 months", "6 months - 7 months", "8 months - 9 months", "9 months - 10 months", "9 months – Newborns", "10 months – Newborns", for width – "5 months - 6 months", "8 months - 9 months", "8 months - 10 months", "9 months - 10 months", "9 months – Newborns", "10 months – Newborns".

Table 2

Length and width of the pancreas head in human fetuses and newborns (mm)

	Pancreas head length		Pancreas head width	
	M±m	Confidence intervals limits	M±m	Confidence intervals limits
4 months	7.02±0.16	6.67-7.37	4.10±0.16	3.74-4.46
5 months	7.86±0.05	7.33-8.39	5.33±0.15	5.01-5.65
6 months	9.34±0.45	8.36-10.32	5.01±0.25	4.48-5.54
7 months	8.46±0.32	7.75-9.17	6.19±0.34	5.44-6.94
8 months	11.14±0.39	10.25-12.03	7.00±0.23	6.47-7.53
9 months	12.82±0.50	11.42-14.22	7.22±0.36	6.23-8.21
10 months	14.02±0.22	13.42-14.62	7.80±0.26	7.08-8.52
Newborns	14.36±0.17	13.96-14.76	8.03±0.08	7.85-8.21

The length of the corpus pancreatic in fetuses and newborns increases from 6.28±0.12 mm (4-month-old fetuses) to 14.84±0.20 mm (neonatal period), while its width – from 4.15±0.16 mm up to 7.17±0.11 mm, respectively (table 3). From the 4th to the 5th month and from the 6th month of fetal development to the neonatal period for the corpus pancreatic length, for its width – from the 4th to the 5th month and from the 6th to the 8th month of fetal development are the two periods of accelerated development, and from the 5th to the 6th month for the corpus pancreatic length and from the 5th to the 6th month and from the 8th month of fetal development to the period of the newborn for its width are the periods of relatively slow development.

According to the results of the Conover-Iman test for the length and width of the pancreas body, the median difference for all possible age pairs is statistically significant, except for its length pairs – "5 months – 6 months", "8 months – 9 months", "9 months – 10 months", "8 months – 10 months", "10 months – Newborns", for width – "5 months – 6 months", "7 months – 8 months", "7 months – 9 months", "8 months – 9 months", "7 months – 10 months", "8 months – 10 months", "9 months – 10 months", "7 months – Newborns", "8 months – Newborns", "9 months – Newborns", "10 months – Newborns".

Table 3

Length and width of the pancreas body in human fetuses and newborns (mm)

	Pancreas body length		Pancreas body width	
	M±m	Confidence intervals limits	M±m	Confidence intervals limits
4 months	6.28±0.12	6.01-6.55	4.15±0.16	3.80-4.50
5 months	8.11±0.29	7.50-8.72	5.12±0.17	4.77-5.47
6 months	8.36±0.34	7.63-9.09	5.36±0.21	4.91-5.81
7 months	9.57±0.40	8.69-10.45	6.56±0.40	5.69-7.43
8 months	12.00±0.52	10.80-13.20	7.07±0.34	6.28-7.86
9 months	13.00±0.25	12.30-13.70	7.02±0.29	6.21-7.83
10 months	13.32±0.37	12.28-14.36	7.44±0.22	6.83-8.05
Newborns	14.84±0.20	14.39-15.29	7.17±0.11	6.92-7.42

During the fetal and early neonatal periods of ontogenesis, the length of the tail of the pancreas increases from 5.16±0.22 mm (4-month-old fetuses) to 8.49±0.27 mm (neonatal period), its width - from 3.62±0, 09 mm to 7.82±0.24 mm, respectively (table 4). There are two periods of accelerated development of the length and width of the tail of the software from the 4th to the 5th month and from the 6th month of fetal development to the neonatal period. From the 5th to the 6th month of fetal development is the period of relatively slow development for the length and width of the pancreas tail.

According to the results of the Conover-Iman test for the length and width of the pancreas tail, the difference in medians for all possible age pairs is statistically significant, except for its length pairs – "5 months – 6 months", "6 months – 7 months", "6 months – 9 months","7 months – 8 months", "8 months – 9 months", "8 months – 10 months", "9 months – 10 months", "7 months – 9 months", "8 months – Newborns ", "9 months – Newborns", "10 months – Newborns", for width – "5 months – 6 months", "6 months – 7 months", "8 months – 9 months", "8 months – 10 months", "8 months – Newborns", "9 months – Newborns", "10 months – Newborns".

Table 4

Length and width of the pancreas tail in human fetuses and newborns (mm)

	Pancreas tail length		Pancreas tail width	
	M±m	Confidence intervals limits	M±m	Confidence intervals limits
4 months	5.16±0.22	4.66-5.66	3.62±0.09	3.42-3.87
5 months	6.42±0.14	6.116.73	4.42±0.16	4.09-4.75
6 months	6.78±0.43	5.86-7.70	4.45±0.16	4.11-4.79
7 months	7.09±0.38	6.25-7.93	5.13±0.39	4.27-5.99
8 months	7.84±0.31	6.11-8.57	7.01±0.36	6.18-7.84
9 months	7.90±0.37	6.87-8.93	7.04±0.17	6.58-7.50
10 months	8.26±0.37	7.23-9.29	7.18±0.14	6.80-7.56
Newborns	8.49±0.27	7.87-9.11	7.82±0.24	7.28-8.36

After correlating all organometric parameters of the pancreas and its anatomical parts during fetal and early neonatal periods of ontogenesis using the Pearson correlation coefficient, it was established that the values of all paired correlation coefficients are quite close to 1 (> 0.74), which indicates the close strong positive correlation between all morphometric parameters.

When comparing the mean values of the pancreas morphometric parameters in all age groups using the Wilcoxon test, it can be stated that all p-values are greater than the significance level $\alpha = 0.05$, which means no significant difference. Thus, based on the arithmetic mean of the pancreas length, we can build a model for predicting the normative values of the organ's morphometric parameters during fetal and early neonatal periods of ontogenesis, using the age of the fetus and newborn and its parieto-calcaneal length.

Model of the pancreas length during the fetal period and in newborns:

Length of the pancreas = β0 + 0.094 x parieto-calcaneal length of the fetus,

where β0: 3.342, if the age period = 4 months; 4.731 = 5 months; 6.924 = 6 months; 10.349 = 7 months; 8.244 = 8 months; 13.821 = 9 months; 17.489 = 10 months; 18.087 = Newborns.

The coefficient of the model determination is 94.18%.

Identification of typical and variant forms of pancreas in fetuses and newborns will help to distinguish its abnormal forms with the subsequent interpretation of morphofunctional features of this organ, which is given in the works of A.V. Smirnov, I.E. Trubitsin [4], S.T. Amann et al. [5]. Studies on the individual anatomical differences amplitude of the pancreas in fetuses and newborns permit to detailize the idea of timing and stages of its morphogenesis after birth. The performed morphological study differs from the well-known ones by the fact that determination of correlations between the pancreas organometric parameters with the subsequent determining the periods of accelerated and delayed development of this organ has important theoretical and practical significance [3, 11].

Designing a model of the pancreas length in fetuses and newborns will help the correct interpretation of perinatal ultrasound and computed tomography. All this plays a crucial role in the prevention of peritoneal pathology. But the concept of the norm for comparison with the actual data of the study is currently a very complex and poorly studied issue [6, 8].

Conclusions

1. In the fetal and early neonatal periods of ontogenesis, the typical form of the pancreas is curved (72±5%), its variant forms are arched (18±4%) and straight (10±2%).

2. The organometric parameters of the pancreas and its anatomical parts of fetuses and newborns are characterized by the two periods of accelerated development and a period of relatively slow development. Periods of accelerated development are: from the 4th to the 6th month and from the 7th month of fetal development to the neonatal period are characteristic of the pancreas length and the length of its head; from the 4th to the 5th month and from the 6th month of fetal development to the neonatal period – for length of the pancreas body and tail and for the width of its head and tail; from the 4th to the 5th month and from the 6th to the 8th month of fetal development – for the width of the the gland's body. Period of relatively slow development is from the 6th to the 7th month of fetal development – for the length of the pancreas and the length of its head; from the 5th to the 6th month of fetal development – for the length of the pancreas body and tail and the width of its head and tail. Only for the width of the gland's body, the second period of relatively slow development from the 8th month of fetal development to the neonatal period is determined.

3. The model for predicting the normative values of the pancreas length morphometric parameters during the fetal and early neonatal periods of ontogenesis is written as: length of the pancreas = β0 + 0.094 x parieto-calcaneal length of the fetus, where β0: 3.342, if the age period = 4 months ; 4.731 = 5 months; 6.924 = 6 months; 10,349 = 7 months; 8.244 = 8 months; 13.821 = 9 months; 17.489 = 10 months; 18.087 = Newborns.

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Стаття надійшла 20.12.2019 р.