

Ovarian vein diameters measured by MDCT in women without evidence of pelvic congestion syndrome

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Abstract

Objective: The purpose of this study was to clarify reference values for ovarian veins diameters in women without evidence of primary or secondary pelvic venous insufficiency and to determine factors influencing these parameters.

Methods: Multidetector computed tomography images and medical records of 197 women were retrospectively reviewed. The patients' age, body mass index and history of parturition were examined.

Results: Diameters of right ovarian veins (ROV) and left ovarian veins (LOV) ranged from one to six mm [mean 2.9 (1.0), 3.2 (1.2), respectively]. The reference values for ROVs diameters were between 0.9 mm and 4.9 mm (95% CI 2.7-3.0 mm), while the reference values for LOVs diameters ranged from 0.8 mm to 5.5 mm (95% CI 3.0-3.3 mm). ROV diameter was significantly narrower than LOV diameter [2.9 (1.0) vs 3.2 (1.2) mm, $p=0.031$]. Ovarian veins diameters were smaller in elderly patients ($p=0.001$ and $p=0.002$), and larger in nulliparous women ($p=0.002$) and those with higher individual frequency of parturition ($p=0.05$). There was a tendency to higher values of veins size in presence of drainage variation. Multiple regression analysis revealed presence of negative significant relationship of ROV size with age, positive association with parturition frequency and anatomical drainage variation of ovarian veins. ROVs and LOVs diameters did not differ in subgroups of normal weight, overweight and obese patients ($p>0.05$).

Conclusion: The present study demonstrated significant reduction of ovarian veins diameters with advancement in age of patients, while increased ovarian veins diameters were related positively to parturition history and higher parturition frequency index. There was a negative relationship of right ovarian veins size with age, and positive association with parturition frequency and drainage variation. Only individual parturition frequency had an independent association with left ovarian vein diameter.

Key words: ovarian vein diameter, women, parturition, parity, multidetector computed tomography

Introduction

Chronic pelvic pain (CPP), defined as a persisting noncyclic dull pelvic pain with duration for more than 6 months, is a common and costly health problem with reported prevalence in the United States of America as 14.7% in young and elderly women (1). The annual prevalence of CPP in the United Kingdom in women aged from 15 to 73 years was found to be 38/1000, a rate comparable to that of asthma (37/1000) and back pain (41/1000) (2). One of the treatable causes of CPP is pelvic congestion syndrome (PCS) (3).

PCS is characterized by non-specific chronic pelvic pain exacerbated by sexual intercourse, postural changes and walking; and is often associated with pelvic varicose veins, congestive dysmenorrhea, dyspareunia, and emotional disturbance (4, 5). The etiology of the primary PCS seems to be related to the reflux in the incompetent and dilated

ovarian veins despite the high prevalence of ovarian vein dilatation and reflux among asymptomatic multiparous women (6-10). The etiology of secondary PCS is related to underlying abnormalities, resulting in increased pressure in the abdominal and pelvic veins, which transmits retrograde to the pelvic venous system resulting in the pelvic congestion (11-12). Although there are no established criteria for the cross-sectional imaging diagnosis of PCS, relatively arbitrary diagnostic criteria are tortuous and dilated ovarian veins, reflux in ovarian veins, congested parauterine and paraovarian venous plexus, and presence of pelvic varicose veins (11, 13, 14). Ovarian vein dilatation with diameters greater than 8 mm on the left side and 4 mm on the right side on multidetector computed tomography (MDCT) are defined as clearly abnormal (11), but this diagnostic criterion is not universally accepted (15).

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There are no cross-sectional imaging studies that reported data regarding to the reference values for ovarian veins size in healthy population. Only few published reports mentioned ovarian vein diameters measured by MDCT or magnetic resonance imaging in symptomatic or asymptomatic patients selected as control group with a relatively small sample size (7, 9, 16, 17).

Multidetector computed tomography is a commonly used diagnostic modality to investigate patients presented with abdominal or pelvic pain. MDCT technique is capable to demonstrate anatomy of the female pelvis, retrograde ovarian venous flow, tortuous and dilated ovarian veins, varicose pelvic veins in asymptomatic women and patients with primary PCS as well as possible sources for secondary PCS (10, 17-19).

The purpose of this single-center retrospective study was to clarify reference values for ovarian veins diameters in women without evidence of pelvic congestion syndrome by means of MDCT and to determine factors influencing these parameters. Furthermore, knowledge of reference values for ovarian veins diameters may be helpful and objective instrumental tool for future investigations of manifestations of PCS.

Methods

Patients and design of the study

Multidetector computed tomography images of 197 Caucasian women without evidence of PCS were retrospectively reviewed for measurements of right ovarian veins (ROV) and left ovarian vein (LOV) diameters. Although MDCT images were reviewed for identifying a location of ovarian veins drainage into renal vein or inferior vena cava (IVC). The study population was selected among consecutive 6544 patients examined by abdominopelvic MDCT for various clinical indications between January 2014 and September 2016 in radiology department of university hospital. Patients with disorders that could influence ovarian vein flow and cause primary or secondary PCS were excluded from the study. Exclusion criteria based on patients' medical records and MDCT images analysis were as following: reflux in ovarian and/or internal iliac veins, tortuous ovarian and/or pelvic veins, presence of varicose veins and venous collaterals in any location, congestive heart failure, obstruction of IVC, obstruction of hepatic or portal veins, cirrhosis, portal hypertension, "nutcracker" phenomenon, circum-aortic or retro-aortic left renal vein, renal vein obstruction, hydronephrosis, acute or chronic kidney diseases, iliac veins obstruction, para-aortic lymphadenopathy, abdominopelvic vascular malformation, abdominal and pelvic masses, history of chronic pelvic pain with duration more than six months, history of pelvic radiation, history of previous abdominopelvic surgery, and postpartum period.

Inclusion criteria for study population were absence of exclusion criteria and clear visualization of both ovarian veins in MDCT images. The patients were divided into 3 age groups:

<49 (111 fertile women, 47.2%), 49-65 (46 non-fertile women age, 32.5%) and >65 years old (40 elderly women, 20.3%) (Table 1). Analyses were also performed for the following groups of patients divided according to the BMI [(normal weight (90 women, 45.5%), overweight (61 women, 30.9%), and obese (46 women, 23.6%)], parity status (parous vs nulliparous; nulliparous, uniparous, and multiparous women) and individual frequency of parturition).

The institutional ethic committee approval for this retrospective study was obtained (institutional record number 34/17). Our institutional ethic committee does not require informed consent from patients for retrospective examination of patients' records and images.

Table 1. Diameters of ovarian veins according to demographic and anthropometric parameters, and reproductive history

Variables	Number of patients, (%)	ROV diameter, mm	LOV diameter, mm
Age groups, years			
<49	111 (47.2)	3.1 (1.0)*	3.2 (1.1)*
49 - 65	46 (32.5)	3.0 (1.0)*	3.3 (1.0)*
>65	40 (20.3)	2.3 (0.1)	2.7 (1.2)
F, p ^a		8.228, <0.001	4.359, 0.014
BMI groups			
Normal	90 (45.5)	2.8 (0.9)	3.1 (1.1)
Overweight	61 (30.9)	3.0 (0.9)	3.1 (1.1)
Obese	46 (23.6)	2.9 (1.2)	3.2 (1.1)
F, p ^a		0.259, 0.772	0.308, 0.734
Parity status			
Nulliparous	51 (25.9)	2.6 (0.7)	2.8 (0.9)
Uniparous	22 (11.2)	3.2 (0.8)	3.1 (1.0)
Multiparous	124 (62.9)	3.0 (1.0)	3.3 (1.2)
Chi-square, p ^b		5.070, 0.079	4.479, 0.106
Nulliparous	51 (25.9)	2.6 (0.7)	2.8 (0.9)
Parous	146 (74.1)	3.0 (1.0)	3.3 (1.2)
t, p ^c		2.399, 0.019 ₋	-2.329, 0.022
Parturition frequency			
Nulliparous	51 (25.9)	2.6 (0.7)**	2.9 (0.8)
<0.50	82 (56.2)	2.9 (1.0)***	3.2 (1.1)
>0.55	64 (43.8)	3.5 (1.0)	3.6 (1.4)
F, p ^a		9.405, 0.009	4.263, 0.119
Data presented as n (%) and mean (SD)			
a - ANOVA test, b - Kruskal-Wallis test, c - t-test for independent samples, d - Mann Whitney U test			
Scheffe posthoc test: * - p<0.05 difference between age group <49 and age group >65 and difference between age group 49 - 65 and age group >65. **p <0.05 for difference between nulliparous women and women with relatively high frequency of births. ***p <0.05 for difference between women with relatively low parturition frequency and women with relatively high parturition frequency.			
BMI - body mass index, LOV - left ovarian vein diameter, ROV - right ovarian vein diameter			

Baseline variable and definitions

Age, weight, height, body mass index (BMI), history of parturition, parturition number, age at first and at last birth, and individual parturition frequency (PF) were noted.

Parturition was defined as number of offspring's female has borne (MESH terms NCBI/NLM/NIH available at www.ncbi.nlm.nih.gov). Parity was defined as a number of complete pregnancies with offspring's; nulliparous - no offspring, uniparous - one offspring born and multiparous - multiple offspring's born) (MESH terms NCBI/NLM/NIH available at www.ncbi.nlm.nih.gov).

The individual parturition frequency (PF) (arbitrary parameter, developed by authors of present study for departmental work and never previously published or clinically validated) was calculated only for multiparous women as individual number of parturition divided by range between corresponded age at the last birth and corresponded age at the first one [e.g. number of parturitions / (age at the last birth - age at first age)]. The PF ranged from 0.18 to 1.00 with bimodal distribution that was present as accumulation of variables between 0.15 to 0.50 and accumulation of variables from 0.55 to 1.00. According to bimodal character of distribution of the PF, all multiparous women were arbitrary divided into two groups; women with relatively less frequent parturition and with relatively high PF (frequency <0.50 and >0.55).

MDCT technique

Multidetector computed tomography examinations were performed with four-channel computed tomography scanners (Asteion 4, Toshiba Medical System Corporation, Japan). The scanning parameters were 5 mm collimation; gantry rotation speed of 0.75 sec; pitch factor of 1.375; helical pitch of 5.5; 120 kVp, and 60-180 mA. One hundred mL of iohexol, 300 mg I/mL (Omnipaque, Amersham Health LTD, Cork, Ireland) were administered intravenously with a power injector at a rate of 4 mL/sec. Biphasic abdominopelvic MDCT scans were done from the upper part of the diaphragm to the pelvic floor with inspiratory breath-holding. Scanning-delay time of the MDCT examination was 15 sec and 70 sec for arterial and venous phase, respectively. Images during arterial phase were used to rule out possible reflux into ovarian veins, and images from venous phase were used for identifying drainage locations of ovarian veins to renal vein or IVC. Reflux into LOV was defined as early opacification of the ovarian vein occurring simultaneously with opacification of the renal veins (7, 10).

Image analysis

All scans were downloaded from DICOM server to workstation, and two radiologists experienced on abdominopelvic and interventional radiology and blinded to patients' clinical data retrospectively examined images on the base of consensus. A

consensus approach was selected because of previously reported high inter-observer agreement for evaluation of detectability of ovarian veins with no significant difference between the two observers' measurements of maximum diameter of ovarian veins by MDCT (16). Assessment of ovarian veins included their diameters and drainage location to renal vein or IVC. Maximum diameters of both ovarian veins were measured in the axial plane. The widest diameters of ovarian veins from two-fold magnified images on monitor using measuring tool were registered. After observing transverse sections by scrolling images for tracking the course of ovarian veins, exact drainage location of ovarian veins also was noted.

Statistical analysis

All continuous data are presented as mean (SD) for normally distributed data or as range and median for abnormally distributed variables. Categorical data are presented as numbers (percentage). Normality of continuous variables distribution was investigated using Kolmogorov-Smirnov test. The reference values for diameters of right and left ovarian veins were calculated separately as (sample mean-1.96 SD) to (sample mean + 1.96 SD). The 95% confidence interval (CI) for both ovarian veins was calculated using sample mean and standard error of sample mean. Analysis of categorical variables was performed using Chi-square test. Comparison of normally distributed continuous variables between two groups was accomplished using t-test for independent samples; while abnormally distributed variables were compared using Mann-Whitney U-test. Comparison of multiple groups was accomplished using one-way ANOVA with post-hoc Scheffe or Bonferroni test for normally distributed data. Kruskal-Wallis test with posttest was performed for multiple groups' comparison of abnormally distributed variables. Multiple linear regression analysis was done for defining the independent variables affecting the size of ovarian veins. The p-value <0.05 was accepted as statistically significant. Statistical analysis was made using IBM SPSS statistical software, version 20 (IBM Corporation, NY).

Results

The patients' age ranged from 18 to 73 years (45.7 (17.1) years). There were 111 patients (47.2%) of <49 years old (fertile women), 46 patients (32.5%) of 49-65 years old (women in menopause) and 40 patients (20.3%) of >65 years old (elderly women). Ninety (45.5%) women had normal weight, while 61 (30.9%) were overweight, and 46 (23.6%) were obese according to the BMI values. Fifty-one (25.9%) patients were nulliparous, 22 (11.2%) were uniparous, and 124 (62.9%) were multiparous. Number of parturitions ranged from one to nine (median 3.0). The age at the first birth ranged from 17 to 43 (median 21) years, while the age at the last birth ranged from 19 to 48 (31.1 (0.4) years). There were 82 (56.2%) women with

individual PF <0.50 and 64 women (43.8%) with individual PF >0.55.

Diameters of ROVs and LOVs ranged from one to six mm (2.9 (1.0) mm, 3.2 (1.2) mm, respectively). The reference values for ROV diameters lied between 0.9 mm and 4.9 mm with 95% CI from 2.7 mm to 3.0 mm, while the reference values for LOV diameters ranged from 0.8 mm to 5.5 mm with 95% CI from 3.0 mm to 3.3 mm.

There was a significant difference between LOVs and ROVs diameters, with ROVs diameters [2.9 (1.0) mm] being significantly narrower than LOVs diameters [3.2 (1.2) mm] for entire patients group ($p=0.031$).

Analysis of ovarian veins diameters according to demographic and anthropometric parameters, history of birth, and anatomic variants related to the drainage location of ovarian veins is presented in Table 1. Comparison of age groups demonstrated that patients >65 years old group had narrower ROVs [2.3 (0.1) mm, $p<0.001$] and LOVs diameters [2.7 (1.2) mm] ($p=0.014$). There were significant differences in ROVs diameters between age groups of <49 years old and >65 years old [3.1 (1.0) mm vs 2.3 (0.1) mm, $p=0.001$] and between 49-65 years old and >65 years old [3.0 (1.0) mm vs 2.3 (0.1) mm, $p=0.002$]. Similarly, LOVs diameters significantly differed between age groups <49 years old and >65 years old [3.2 (1.1) mm vs 2.7 (1.2) mm, $p=0.044$] and between age groups <49-65 years old and >65 years old [3.3 (1.0) mm vs 2.7 (1.2) mm, $p=0.021$]. Differences for ROVs and LOVs diameters between age groups <49 years old and 49-65 years old were not significant ($p>0.05$ for both) (Table 1).

Analysis of ovarian vein diameters according to BMI values showed absence of difference in ROVs and LOVs diameters in subgroups of normal weight, overweight and obese patients ($p>0.05$ for both) (Table 1).

There was a tendency in ROVs and LOVs diameters to be increased in uniparous and multiparous women compared to nulliparous one, but these differences did not reach statistical significance ($p=0.079$, $p=0.106$, respectively). On other hand, when patients were grouped as parous and nulliparous, ROVs and LOVs appeared to be significantly wider in parous women compared with nulliparous ($p=0.019$, $p=0.022$, respectively) (Table 1).

Comparison of mean ovarian vein diameters in groups with different PF in parous and nulliparous women showed increased ROVs and tendency to higher LOVs diameters in women with relatively high PF as compared with relatively lower PF and nulliparous women ($p=0.009$, $p=0.119$, respectively). ROVs diameters were significantly wider in women with PF >0.55 than in those with PF<0.50 and nulliparous women ($p=0.018$, $p=0.002$, respectively). There

was a tendency for wider LOVs diameter in women with relatively high PF compared with those in nulliparous women ($p=0.055$), while no difference was observed between PF groups ($p>0.05$). Nulliparous patients and patients with relatively low PF did not differ as regards to ROVs and LOVs diameters ($p>0.05$ for both) (Table 1).

Diameters of ROVs drained into unilateral renal vein [3.6 (1.3) mm; 12 patients, 6.09%] seemed to be wider than diameters of ROVs drained directly to the IVC [2.9 (1.0) mm; 184 patients, 93.91%], but difference was not significant ($p=0.06$). In addition, diameters of LOVs drained into unilateral renal veins by single junction [3.2 (1.4) mm; 191 patients, 96.95%] had tendency to be narrower than diameters of LOVs drained to left renal veins via multiple drainage junctions [4.0 (0.8) mm; 6 patients, 3.05%], but difference was not significant ($p=0.287$). The only patient with LOV drained directly to the IVC but not to the left renal vein was not included into this study.

Multiple regression analysis of factors that can affect ovarian vein size (Table 2) demonstrated significant association of ovarian veins diameter with age, PF and anatomic location of drainage, while individual PF and BMI values did not affect vein diameter. There was a negative significant association of ROVs diameters with increase of the age ($\beta=0.292$, $p=0.024$), while both ovarian veins diameters were positively associated with increase of PF (ROV- $\beta=0.359$, $p<0.001$, and LOV- $\beta=0.247$, $p=0.014$). Results of multiple linear regression analysis showed that anatomical drainage variations of ovarian veins into renal veins was the significant factor influencing ROVs diameters ($\beta=0.182$, $p=0.028$), but not LOV diameter ($\beta=0.055$, $p=0.637$).

Table 2. Multiple regression analysis of the association between clinical and anatomical variables and ovarian veins diameters

Variables	Standardised Beta coefficient	p
ROV		
Age	-0.292	0.024
BMI	0.058	0.565
Parturition number	0.008	0.951
Parturition frequency	0.359	<0.0001
Variant of ROV drainage	0.182	0.028
LOV		
Age	-0.182	0.182
BMI	0.126	0.249
Parturition number	-0.073	0.595
Parturition frequency	0.247	0.014
Variant of LOV drainage	0.055	0.525

BMI - body mass index, ROV - right ovarian vein, LOV - left ovarian vein

Discussion

This study, performed on the relatively large population with sample size of 197 women selected from 6544 patients, demonstrated that upper limits for ROVs diameters should be close to 4.9 mm, and upper limits for LOVs diameters should be close to 5.5 mm in women without evidence of PCS. Our findings are in concordance with previous MDCT study that investigated relationship between ROV variance with pelvic varices and reported similar mean diameters of ROVs and LOVs in parous and nulliparous women without pelvic varices (9). However, another study reported a larger ovarian vein sizes [ROV 4.4 (0.5) mm, LOV 5.2 (1.0) mm] measured by the magnetic resonance imaging. These differences seem to be due to smaller sample size of their study population (22 potential kidney donors) (9). Another study also reported slightly larger mean diameters of ovarian veins [ROV 4.2 (1.2) mm, LOV 4.9 (1.3) mm] in asymptomatic women without reflux in ovarian veins on MDCT scans (7). This contradiction probably may be related to regional or ethnic differences between Asian and Caucasian patients groups.

There was a significant difference between LOV and ROV diameters in our study population, with ROV diameter being significantly narrower than LOV diameter for entire study population. These findings are contrary to data from previously published study that investigated ovarian veins by MDCT in patients with large pelvic masses (16). This discordance may be due to different sample size of their control and patients groups. The difference between LOVs and ROVs diameters in women without PCS might be related to their different drainage location. ROV typically drains directly to IVC by acute angle, while LOV joins left renal vein by right angle and then it finally drains to IVC (21). Hence, the more indirect path of the LOV to the IVC via left renal vein seems to be an important factor causing a wider LOV diameter.

The present study demonstrated significant reduction of ROVs and LOVs diameters with increase of women's age. One previously published study reported smaller calibers of gonadal veins in younger women compared with those in elderly patients on MDCT scans of patients with large pelvic masses. The smaller diameters in young women were detected in both patients and controls groups, which were divided into three different age groups (≤ 30 , 31-59, and ≥ 60 years old) (16). A contradiction with results of presented study may be related to different division of patients according to patients' age. Additionally, the difference may be explained by parity status of the women included in our study, most of our patients (74.1%) were parous. However, authors of above-mentioned study did not report the parity status of their patients. Reduction of ovarian vein diameters with increase of patients' age seems to be associated with involution of reproductive organs.

Additionally, our study demonstrated that parturition history resulted in increase of ovarian vein diameters. These findings are in concordance with previously reported MDCT studies that described larger ovarian vein size for each side in parous women (7, 17).

The results of this study showed increased ROVs diameters and tendency to wider LOVs diameters in women with relatively higher PF that in women with relatively lower PF and nulliparous women. Although a positive association between parity status and increase in ovarian vein size is well known (10, 17), to our knowledge, there were no published reports about influence of individual PF on ovarian vein diameters in women without evidence of PCS. This result allows suggesting higher individual frequency of births as an important factor influencing ovarian vein size in healthy women.

There was a tendency to higher values of ovarian veins diameters regarding to anatomic variations of veins drainage. Diameters of ROVs drained into unilateral renal vein tend to be wider than those directly drained to the IVC, and diameters of LOVs drained into left renal veins via multiple junctions had tendency to be wider than diameters those drained by single junction. Previously reported studies did not found any difference in ovarian vein size according to drainage location (7, 17). This contradiction may be explained by low incidence of anatomical variations of ovarian veins drainage location or type of junction, especially for LOVs. Most frequently, there is a single LOV entering left renal vein. Less frequently, two or more small accessory channels from proximal portion of LOV may drain separately into renal vein (21).

An important finding of this study is that among factors affecting LOV diameter, only individual PF has an independent association with vein diameter. As mentioned previously, contrary to ROV, left ovarian vein joins left renal vein by right angle and then it finally drains to IVC (21). To our opinion, the more indirect path of the LOV to the IVC via left renal vein causes enlargement of LOV diameter; hence, other factors cannot influence already normally enlarged LOV.

The strength of this study was the large study population of 197 women without evidence of PCS selected from consecutive 6544 patients. The exclusion criteria for present study were appropriately selected, and inclusion criteria were defined as clear as possible. We proposed reference values for ovarian veins diameters measured by means of MDCT and described large scale of factors affecting the ovarian vein size.

Study limitations

There are several limitations of our study. Firstly, due to retrospective analysis of medical database some patients with undocumented history of chronic pelvic pain with duration more than six months or history of previous endometriosis

and pelvic inflammatory disease might be included in study population. Secondly, evaluation of ovarian vein diameters by two radiologists based on consensus approach may lead to systematic error of measurements. Finally, a small number of patients with variants of ovarian vein drainage location must be acknowledged. Thirdly, another possible important limitation is using of home-made arbitrary parameter such as individual frequency of parturition that was never clinically validated.

Further investigations are needed to evaluate specificity and sensitivity of proposed reference values of ovarian vein diameters in comparison with patients with PCS for definitive cut-off values of ovarian veins diameters. Additional studies with larger number of patients with variants of LOVs drainage via multiple venous channels to left renal vein and those for LOV directly drained to IVC will clarify influence of anatomic variation on ovarian vein diameters in healthy women. In addition, external validation of clinical importance of individual frequency of parturition parameter is warranted.

Conclusion

In women without pelvic congestion syndrome, upper limits for ROVs diameters were close to 4.9 mm, and upper limits for LOVs diameters were closed to 5.5 mm. The present study demonstrated significant reduction of ovarian veins diameters with increase of patients' age, while parturition history and higher individual parturition frequency resulted in increase of ovarian veins diameters. Negative relationship of right ovarian veins size with age, and positive association with parturition frequency and drainage variation was shown. Only individual parturition frequency had an independent association with left ovarian vein diameter.

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