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Computed tomography identifies sex-specific differences in surgical chronic thromboembolic pulmonary hypertension

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BACKGROUND: Registry data suggest women are less likely than men to undergo pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension despite a similar proportion of proximal vs distal disease. We hypothesized that sex-specific differences could be elicited with a computed tomography pulmonary angiography analysis beyond proximal vs distal.

METHODS: Preoperative computed tomography pulmonary angiography of patients who underwent pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension from January 2017 to September 2021 was analyzed. The pulmonary vascular tree was divided into 32 named vessels with chronic thromboembolism presence and lesion type recorded for each vessel. If no lesion was identified in a segmental vessel, subsegmental disease was recorded when present.

RESULTS: One hundred forty-four patients (mean age 57 ± 15 years, 78 women) were included. There were no sex differences in baseline hemodynamics. Men had more vessels involved than women (mean 20.3 vs 17.1, $p = 0.004$) and had fewer disease-free pulmonary segments (mean 4.9 ± 4.3 vs 7.6 ± 5.5, $p = 0.001$). Men had a greater number of webs, eccentric thickening, and occlusions. The distribution of lesion type did not significantly differ between sexes at the main or lobar level but men had significantly more lesions in the segmental vasculature while women had a higher proportion of subsegmental lesions ($p < 0.001$).

CONCLUSIONS: Sex-specific differences in chronic thromboembolic pulmonary hypertension are demonstrated on computed tomography pulmonary angiography in overall distribution and lesion type at the segmental and subsegmental level with women having fewer and more distal lesions despite similar hemodynamics.
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Background

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare but increasingly recognized disease estimated to occur in around 3% of acute pulmonary embolism survivors within 2 years.[1] The optimal treatment for CTEPH is pulmonary endarterectomy (PEA) in which the chronic thromboemboli are surgically extracted.[2,3] Outcomes for patients who undergo PEA are excellent with low operative mortality at experienced centers and excellent long-term survival.[3-6] However, registry data have recently revealed sex-specific disparities in who is offered surgery.[7,8] Identifying the cause of this disparity is particularly important as patients with CTEPH are already subject to delays in diagnosis and treatment.

In the European CTEPH registry, women were less likely to be operated on than men (54% vs 65%, respectively), and this difference was accentuated at low-volume centers.[7] Reasons for not operating on women were reported to include a concern for microvascular disease and older age, despite an overall lower burden of comorbidities. A further study examining sex differences in patients from a Spanish CTEPH cohort also noted that women were less likely to be operated on than men.[8] The authors thus hypothesized that the pattern of CTEPH may differ between the sexes yet both the European and Spanish studies demonstrated no significant difference in the distribution of chronic thromboemboli on imaging. However, the imaging findings in both studies only categorized chronic thromboemboli in a binary classification as proximal or distal.

The proximal or distal distinction stems from the new University of California San Diego (UCSD) surgical classification scheme of CTEPH,[9] whereby the single most proximal chronic thromboembolic lesion determines the level of disease (level 1—main vessels; level 2—lobar vessels; level 3—segmental vessels; level 4—subsegmental vessels). Historically, disease in the distal segmental and subsegmental vasculature was considered distal and inoperable, but this is increasingly less relevant as the margins of what is operable have become blurred. Furthermore, multimodality treatment using balloon pulmonary angioplasty[10] and medical therapy[11,12] are increasingly engaged offering further options for those less suitable for surgical management.

The preoperative imaging evaluation of patients with CTEPH usually involves computed tomography pulmonary angiography (CTPA) and the findings on CTPA correlate well with the surgical level of disease.[13,14] Thus, while digital subtraction angiography is the gold standard imaging test for the diagnosis of CTEPH, it can be substituted by high-quality CTPA in most cases.[14,15] While both the European CTEPH registry[7] and the Spanish experience[8] did not find significant differences in imaging between the sexes in chronic thromboembolism distribution, we sought to determine whether a more detailed CTPA analysis, beyond the proximal/distal distinction, could demonstrate sex-related differences in chronic thromboembolism lesion type and distribution in CTEPH.

Materials and methods

Eligibility

This single-center retrospective study obtained institutional research ethics board approval (REB# 22-5343) and waiver of patient consent. We analyzed adult patients who underwent PEA for CTEPH in our institution between January 2017 and September 2021. The diagnosis for each patient was confirmed in a multidisciplinary setting involving a thoracic radiologist, thoracic surgeons with expertise in PEA, a respirologist with expertise in pulmonary hypertension, an interventional radiologist with expertise in balloon pulmonary angioplasty (BPA), and allied health personnel.[15,16] Clinical data collected from the medical record for each patient included baseline characteristics, preoperative hemodynamic parameters from right heart catheterization, comorbidities, and UCSD surgical level. An individual's sex is classified according to the permanent medical record demographic data, which is sourced from the individual's provincial health insurance and by default sex assigned at birth unless changed by the individual.

Patients were excluded from the study if (1) they did not have a CTPA performed within 100 days before surgery, (2) their CTPA was of insufficient quality (due to respiratory motion obscuring segmental level vessels, minimum slice thickness ≥2 mm, or suboptimal contrast opacification < 200 Hounsfield units measured in the main pulmonary artery), (3) the right heart catheter data were not available, or (4) they underwent simultaneous surgeries (e.g., for congenital heart disease) at the time of PEA (Figure 1).

Imaging protocols

All patients considered for PEA at our center must undergo several imaging examinations, which include, at a minimum, chest radiography, ventilation-perfusion scintigraphy, and a CTPA study.[15] The usual protocol at our institution for a patient with pulmonary hypertension would be to perform a posteroanterior and lateral chest radiograph, ventilation-perfusion scintigraphy as a screening test, and, if positive, a CTPA study for confirmation of CTEPH. In patients considered for PEA, catheter angiography is reserved for cases where CTPA is poor quality or there is diagnostic uncertainty and, with increasing experience in interpreting CTPA, preoperative catheter angiography has become uncommon but this is heavily dependent on local expertise.

Although techniques vary, at our institution, CTPA was typically performed on an 80-slice scanner (Aquilion Prime, Canon) during suspended respiration following injection of 70 cc of iodinated contrast (Ultravist 370; Bayer Healthcare, Berlin, Germany) at 5 ml/s via an 18G antecubital intravenous catheter. Image acquisition was triggered at 200 to 250 Hounsfield units using a bolus tracking technique with a region of interest placed over the main pulmonary artery. The standard voltage was set at 120 kV,

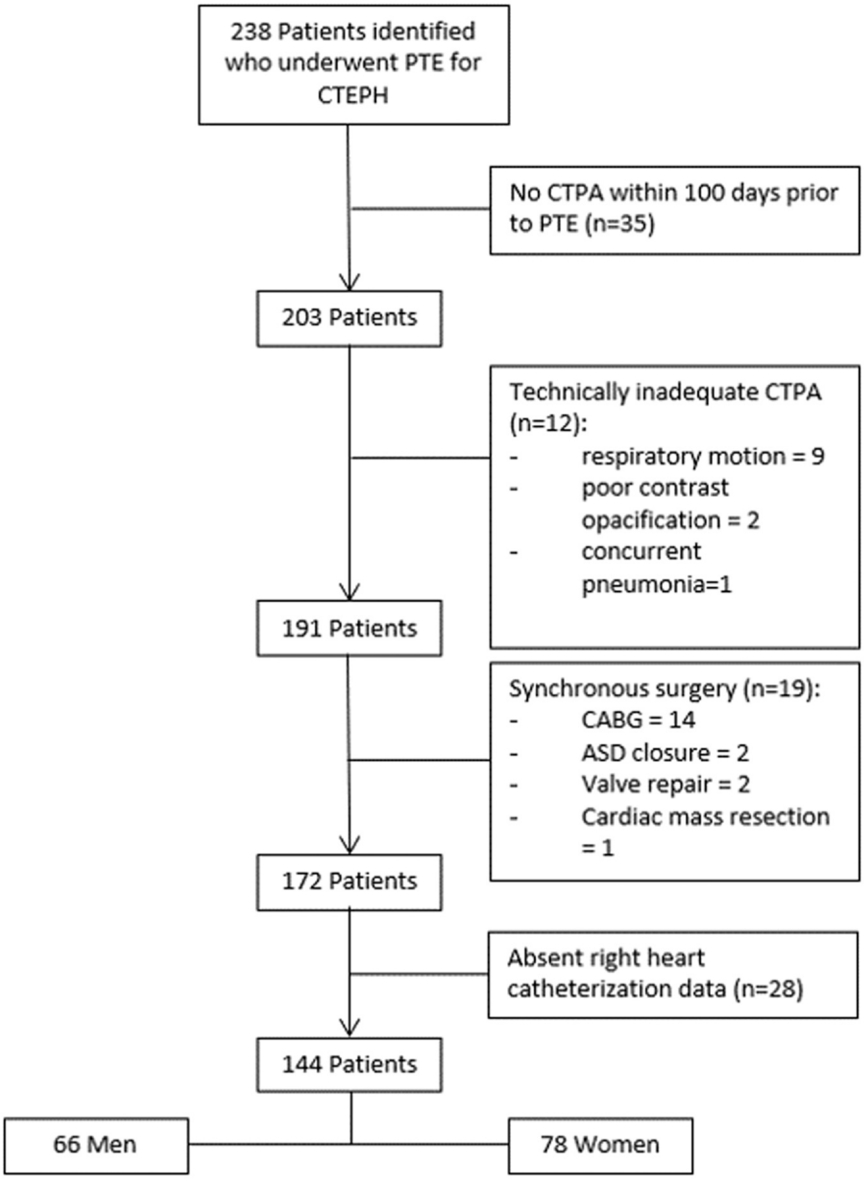

Figure 1 Flowchart demonstrating patient selection. ASD, atrial septal defect; CABG, coronary artery bypass grafting; CTEPH, chronic thromboembolic pulmonary hypertension, CTPA, computed tomography pulmonary angiography, PTE, pulmonary thromboendarterectomy.

though it may be adjusted according to patient weight, and automated exposure control was used to optimize patient dose received. Images were reconstructed in 0.5- to 1.0-mm thick transverse slices using a mediastinal kernel. Coronal and sagittal reformats were performed with 1-mm thick slices using a mediastinal kernel. Due to the tertiary nature of a PEA, some patients had preoperative imaging performed at other institutions but all studies underwent preliminary review for technical adequacy as described above.

Image analysis

The CTPA for each patient was reviewed on the picture archive and communications system (Coral Viewer, Ontario, Canada) and analyzed by a fellowship-trained thoracic radiologist with expertise in CTEPH (M.M.), blinded to the purpose of the study, using a previously reported technique.[12] In brief, the pulmonary vasculature was evaluated as 32 distinct named vessels per patient, comprising vessels to the level of the segmental arteries (3 main, 5 lobar, 1 interlobar, 2 basal trunks, 1 lingular, and 20 segmental pulmonary arteries). Each of the 32 named vessels was evaluated for findings of chronic thromboemboli, including an arterial web, eccentric wall thickening, or a complete occlusion (Figure S1). If there was more than 1 lesion present in a vessel, the most occlusive lesion was recorded (occlusion > eccentric thickening > web). If a segmental artery was clear of disease, the subsegmental arteries supplied by that vessel were evaluated and subsegmental disease was recorded as present or absent. Subsegmental vessels were not classified by lesion type due to limitations in accurately assessing small vessels and they frequently present as narrow caliber or pruned vessels. Due

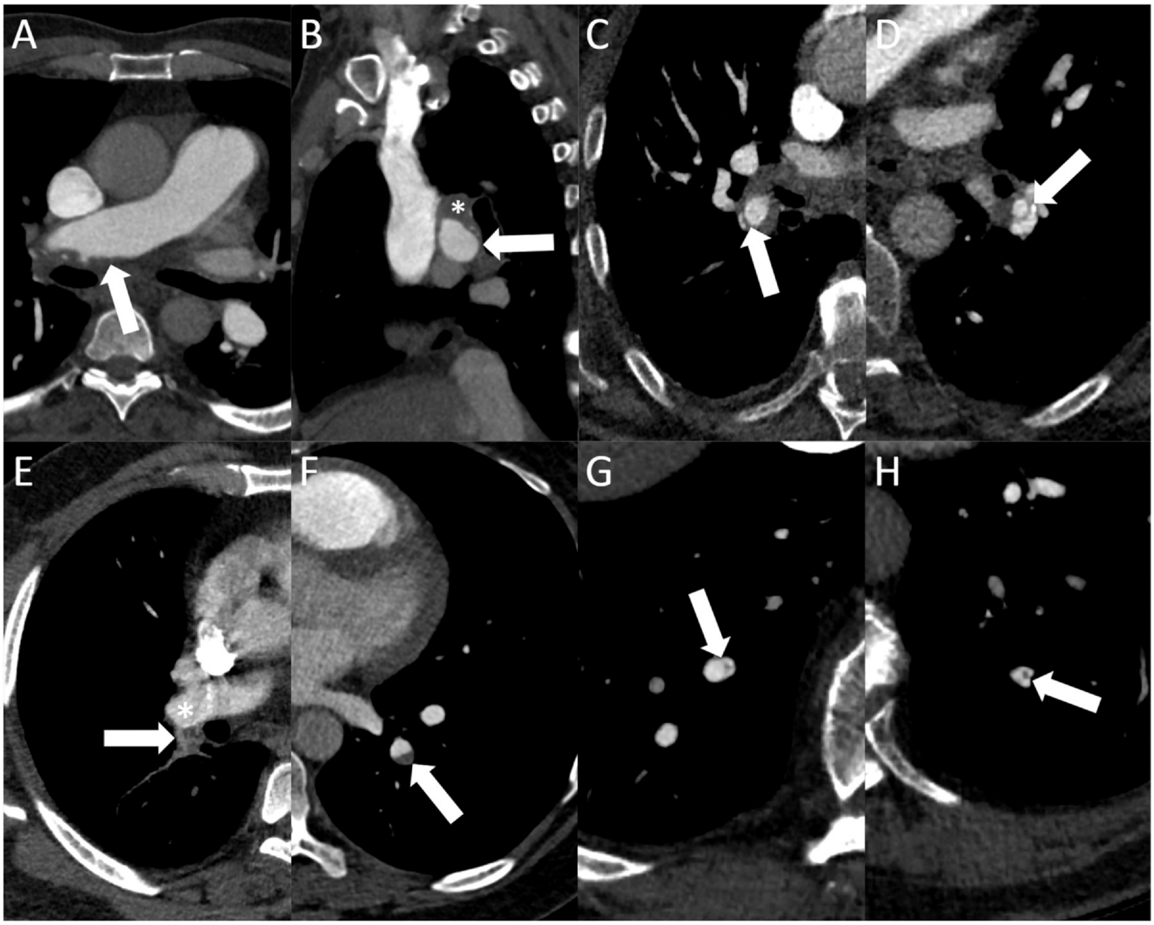

Figure 2 Spectrum of chronic thromboembolic disease encountered on CT pulmonary angiography. (A) Chronic thromboembolism often manifests as eccentric thickening in the proximal vasculature as seen in this 57-year-old man where layering thrombus (arrow) is seen along the posterior wall of the right main pulmonary artery extending into the interlobar pulmonary artery. (B) Sagittal reformat in the same patient demonstrates complete occlusion of the right upper lobe pulmonary artery which is now seen as a thrombosed pouch-like defect (asterisk) superior to the right main pulmonary artery (arrow). (C) The descending branch of the right lower lobe is a common site of disease as seen in this 60-year-old woman where a web is visible across the lateral aspect of the vessel (arrow) and a similar web is also seen in the contralateral lobe (arrow, D). (E) The most common lesions are segmental as seen in this 53-year-old man with a complete occlusion of the right lower lobe superior segment (arrow), flush with the interlobar vessel (asterisk). (F) Eccentric thickening can also be seen at the segmental level as demonstrated here in the posterior basal left lower lobe in a 45-year-old woman. Subsegmental lesions are the most challenging to identify but are well demonstrated here in the posterior basal right lower lobe (G, arrow) and left lower lobe (H, arrow) in a 77-year-old woman. CT, computed tomography.

to anatomic variations, some patients had fewer than 32 vessels (e.g., separate origin of the middle lobe segmental vessels from the interlobar pulmonary artery) and, for analysis purposes, these were recorded as no disease for a constant denominator of 32.

The total number and type of chronic thromboembolic lesions per case were calculated and compared between men and women. Examples of chronic thromboembolic lesion type and level are included in Figure 2. Similar to the UCSD surgical classification, the number and type of lesions were compared between men and women at each computed tomography (CT) level with level 1 corresponding to disease in the main pulmonary arteries, level 2 the lobar vessels, level 3 the segmental vessels, and level 4 the subsegmental vessels.[9,13,17]

The disease distribution and morphology were used to calculate 2 previously described thromboembolic scores. The first of these was the Qanadli index, modified for chronic thromboembolic disease by Hoey et al and termed the CT obstruction index.[18,19] The CT obstruction index quantifies the extent of vascular obstruction expressed as a percentage of normal. Second, the CT level of disease (range 1-4) was also calculated for each patient based on the single most proximal lesion identified.[9,13,17]

Statistical analysis

Continuous variables are reported as means with standard deviations. Differences between groups were evaluated using Student's t-test or Mann-Whitney U test after testing for normality. Differences in categorical variables were evaluated using a chi-square test or Fisher's exact test, where appropriate. Kendall's tau was used to compare the CT level of disease with UCSD level. A p-value < 0.05 was considered statistically significant.

Results

Patient characteristics

Overall, 144 patients were included in the analysis with more women ($n = 78$, 54%) than men ($n = 66$, 46%). Excluded patients were of a similar proportion of women as the included cohort (50% vs 54%, $p = 0.54$). The mean patient age was 56.6 ± 15 years and most were functionally New York Heart Association class III or class IV before their surgery. Right heart catheterization revealed an average mean pulmonary arterial pressure of 42.7 ± 12.8 mm Hg. There were no significant differences between men and women in terms of baseline characteristics, right heart catheterization values, including pulmonary vascular resistance in men vs women (7.1 ± 3.8 vs 8.1 ± 5.5 Wood units, $p = 0.53$) and cardiac index (2.1 ± 0.5 vs 2.3 ± 0.6 liter/min/m^2, $p = 0.052$), or UCSD surgical level (Table 1). Men were more likely to report a history of smoking ($p = 0.03$), coronary artery disease ($p = 0.04$), and more women reported thyroid disease ($p = 0.01$). There was a nonsignificant trend for men to have reported more episodes of venous thromboembolism (Table S1).

Anatomic distribution

A total of 4,562 vessels (2,089 in men and 2,473 in women) were analyzed and a total of 2,679 lesions were identified (1,342 in men vs 1,337 in women). Most patients (79%) had involvement of all five lobes and the left upper lobe was less frequently involved in women (Table 2). The most common lobe involved in both sexes was the right lower lobe in 98% of cases and least common in both sexes was the right middle lobe in 89% of cases overall. Of the 32 named vessels analyzed, the most common vessels involved were the right lower lobe lateral basal and posterior basal

Table 2 Distribution of Overall Disease

Distribution	Men ($n = 66$)	Women ($n = 78$)	p-value
Lobar distribution			
Total involved lobes	4.79 ± 0.57	4.54 ± 0.92	0.07
Right upper lobe	0.95 ± 0.21	0.91 ± 0.29	0.3
Right middle lobe	0.92 ± 0.27	0.86 ± 0.35	0.22
Right lower lobe	0.98 ± 0.12	0.97 ± 0.16	0.67
Left upper lobe	0.97 ± 0.17	0.87 ± 0.34	0.04
Left lower lobe	0.95 ± 0.21	0.92 ± 0.27	0.44
CT level of disease			0.46
1 (n, %)	17 (25.8)	15 (19.2)	
2 (n, %)	36 (54.5)	40 (51.3)	
3 (n, %)	12 (18.2)	19 (24.4)	
4 (n, %)	1 (1.5)	4 (5.1)	

Abbreviation: CT, computed tomography.
Values are expressed as mean ± standard deviation unless otherwise specified. Data in parentheses are percentages.

Table 1 Baseline Characteristics Comparing Men and Women

Characteristic	Men ($n = 66$)	Women ($n = 78$)	p-value
Age (years)	58.3 ± 11.7	55.1 ± 17.4	0.46
BMI	29.8 ± 6.3	32.8 ± 9.4	0.06
6MWT% predicted	72.3 ± 24.9	67.9 ± 21.6	0.12
BNP	252.7 ± 440.7	264.8 ± 379	0.63
NYHA class			
I/II	21 (33.3)		
III/IV	42 (66.6)	58 (78.4)	0.12
I/II	21 (33.3)	16 (21.6)	
III/IV	42 (66.7)	58 (78.4)	
UCSD surgical level (n,%)			0.16
1	16 (24.2)	16 (20.5)	
2	26 (39.4)	19 (24.4)	
3	21 (31.9)	35 (44.9)	
4	2 (3.0)	5 (6.4)	
Right heart catheterization			
mPAP (mm Hg)	41.1 ± 12.2	44.0 ± 13.1	0.27
PVR (Wood units)	7.1 ± 3.8	8.1 ± 5.5	0.53
PCWP (mm Hg)	12.4 ± 6.9	13.2 ± 7.4	0.45
Cardiac index (liter/min/m^2)	2.1 ± 0.5	2.3 ± 0.6	0.05
Pulmonary function[a]			
FEV1 (%predicted)	82 ± 16	79 ± 13	0.38
DLCO (%predicted)	74 ± 14	74 ± 15	0.99
FEV1/FVC ratio	0.70 ± 0.11	0.75 ± 0.10	0.06

Abbreviations: 6MWT, 6-minute walk test; BMI, body mass index; BNP, B-natriuretic peptide; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV1, forced expiratory volume in 1 sec; FVC, functional vital capacity; NYHA, New York Heart Association; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; PCWP, pulmonary capillary wedge pressure; UCSD, University of California San Diego.
Values are expressed as means ± SD unless otherwise specified. Data in parentheses are percentages.
[a]Available in 82 patients.

segmental arteries (both $n = 133$, 92%). The least common vessels involved were the main pulmonary artery, involved in only 9 cases (6.2%), followed by the left main pulmonary artery involved in 11 cases (7.6%). The most and least commonly involved vessels were the same for both sexes. However, the total number of vessels involved was higher in men than in women (20.3 vs 17.1, $p = 0.004$). There were 4 cases of unilateral disease (3 cases with right lung involvement and 1 with left lung involvement) between 1 man and 3 women.

CT level of disease

There was no significant difference in the CT level of disease between men and women when calculated according to the single most proximal lesion identified. When grouping CT level of disease as proximal (levels 1 and 2) vs distal (levels 3 and 4), there was also no significant difference between men and women (Table 2). The CT level of disease was strongly correlated with the UCSD level (Kendall's tau: 0.71).

The total number of chronic thromboemboli at each level was then evaluated and the distribution of chronic thromboemboli across the levels was compared between men and women. There was no significant difference between men and women at level 1 (main vessels, $p = 0.8$) and level 2 (lobar vessels, $p = 0.7$) (Table 3). Men had a greater proportion of their total lesions located at level 3 than women (70.1% vs 62.4%, $p < 0.001$). Subsegmental lesions, level 4, accounted for a greater proportion of disease in women than men (27.2% vs 19.0%, $p < 0.001$).

Type of chronic thromboembolism lesion

Webs were the most common lesion type in both sexes with 977 webs identified overall (36.5% of all lesions). In men, webs made up a greater proportion of all diseases than in women (39.3% vs 33.7%, $p = 0.003$) and, as above, women had a greater proportion of subsegmental lesions (27.2 vs 19.0%, $p < 0.001$). There was no significant difference in the proportion of disease accounted for by eccentric thickening and occlusions (Table 3).

Thromboembolism lesion type by level

The most common lesion types observed at the main and lobar level were eccentric thickening, then occlusion, with no difference between men and women (Table 4). Solitary webs in these large caliber vessels were uncommon. However, at the segmental level, there was a distinct propensity for web formation as they were the most common lesion observed overall and these were more numerous in men than women (Figure 3). Occlusions were more common than eccentric thickening at the segmental level.

Chronic thromboembolism quantification

When the CT obstruction index was calculated for each patient, there was a small but statistically significant difference in the degree of overall arterial obstruction in men compared with women with men having 51.7 ± 13.4% of the vascular bed being obstructed compared with a mean score of 44.7 ± 16.9% in women ($p = 0.007$).

Discussion

A detailed analysis of chronic thromboembolic lesions identified sex-specific differences in surgical CTEPH. Our work confirmed prior reports that simple classification of chronic thromboembolism as proximal vs distal would not elicit differences between the sexes despite a prevailing sentiment that women and men may present differently clinically. While both sexes presented with diffuse disease, men had a greater number of vessels involved at presentation and this difference principally manifested in the segmental arteries with men having more webs, eccentric thickening, and pulmonary artery occlusions at that level. In contrast, women had a greater proportion of their lesions at the subsegmental level. The number and distality of chronic thromboembolic lesions directly impact the surgical

Table 3 Distribution and Lesion Type

Distribution/lesion type	Men ($n = 1342$)	Women ($n = 1,337$)	p-value
Distribution by CT level			< 0.001
Level 1 (main pulmonary arteries)	23 (1.7)	22 (1.6)	0.89
Level 2 (lobar/interlobar arteries)	123 (9.2)	117 (8.8)	0.71
Level 3 (segmental arteries)	941 (70.1)	834 (62.4)	< 0.001
Level 4 (subsegmental arteries)	255 (19.0)	364 (27.2)	< 0.001
Proportions of lesions by type			< 0.001
Web	527 (39.3)	450 (33.7)	0.003
Eccentric thickening	267 (19.9)	254 (19.0)	0.59
Occlusion	293 (21.8)	269 (20.1)	0.3
Subsegmental	255 (19.0)	364 (27.2)	< 0.001

Abbreviation: CT, computed tomography.

Data in parentheses are percentages. A chi-square test was used to determine if the distribution of lesion level and type differs between the sexes. Chi-square tests were additionally conducted separately for each lesion type (e.g., webs vs no webs).

Table 4 Thromboembolism Type by Level

Level and lesion type	Men ($n = 66$)	Women ($n = 78$)	p-value
Level 1 (main pulmonary arteries)	$n = 198$	$n = 234$	0.74
Web	1 (0.5)	0(0)	
Eccentric thickening	19 (9.6)	19 (8.1)	
Occlusion	3 (1.5)	3 (1.3)	
No lesion	175 (88.4)	212 (90.6)	
Level 2 (lobar/interlobar arteries)	$n = 374$	$n = 449$	0.14
Web	9 (2.4)	11 (2.4)	
Eccentric thickening	81 (21.7)	80 (17.8)	
Occlusion	33 (8.8)	26 (5.8)	
No lesion	251 (67.1)	332 (73.9)	
Level 3 (segmental arteries)	$n = 1,517$	$n = 1,790$	< 0.001
Web	517 (34.1)	439 (24.5)	
Eccentric thickening	167 (11.0)	155 (8.7)	
Occlusion	257 (16.9)	240 (13.4)	
No lesion	576 (38.0)	956 (53.4)	
Level 4 (subsegmental arteries)	$n = 576$	$n = 956$	0.02
Subsegmental lesion	255 (44.3)	364 (38.1)	
No lesion	321 (55.7)	592 (61.9)	

Values are expressed as total number of chronic thromboembolic lesions. Data in parentheses are percentages. Chi-square tests were used to compare the distribution of chronic thromboembolism type at each level of disease.

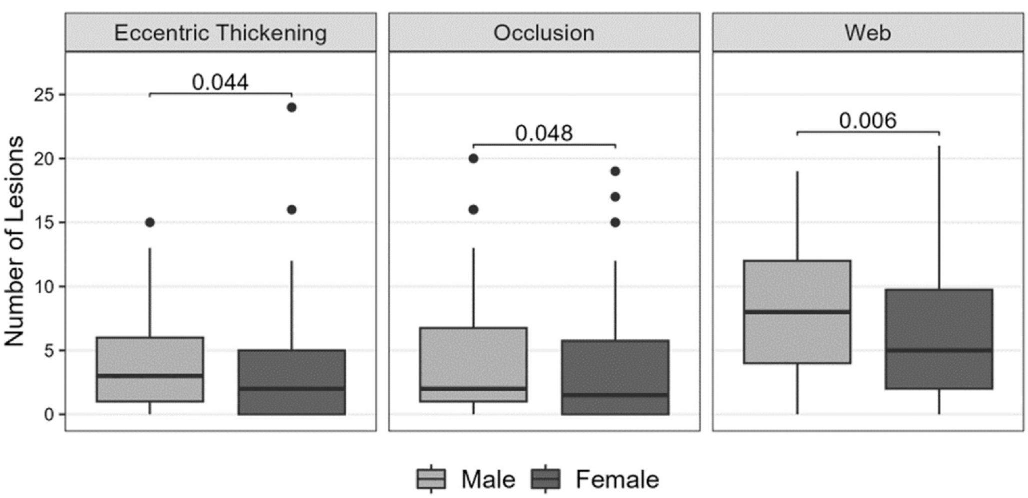

Figure 3 Box and whisker plots of total number of chronic thromboembolic lesions identified per case at the segmental level in men compared to women. Men had more of each lesion type.

management of patients with CTEPH and we postulate that differences in disease quantification and distality may in part account for sex-related disparities in CTEPH management.

To date, analysis of the sex-specific differences in CTEPH patients has focused primarily on risk factors, clinical phenotypes, and treatment outcomes with limited data on the differences in radiological findings between the sexes.[7,8] Analysis of imaging findings in earlier studies has been limited to the categorization of disease as either proximal or distal with no observed differences between the sexes. When the imaging of patients in our study was analyzed using a similar approach (proximal vs distal disease), we also observed no significant differences between men and women suggesting our patient cohort was similar to those in other studies and this is also reflected in the baseline clinical characteristics and comorbidity data.[7,8] However, what these earlier studies have shown is that women are less likely to undergo PEA than men and that overall women have better survival outcomes, although women experience higher operative PEA mortality and a greater need for medical therapy post-PEA.[7,20,21] These differences hint at the potential existence of different phenotypes among CTEPH patients, which may align with sex.

The European CTEPH registry found that women were less likely than men to undergo PEA overall and particularly at low-volume centers.[7] Our findings of an increased proportion of subsegmental lesions in women may indicate a higher degree of surgical difficulty in performing a PEA and we hypothesize that this contributes to the exaggerated difference, particularly in low-volume centers. Indeed, access to subsegmental lesions requires longer periods of deep hypothermic circulatory arrest which can extend up to 50 to 55 minutes on average with up to 3 periods of circulatory arrest of 20 minutes each.[9,22,23] In patients with more subsegmental disease, it is possible that surgical teams with less experience may perceive the severity of the pulmonary vascular resistance to be out-of-proportion to the degree of chronic thromboembolic disease and thus exclude these patients from surgery. Paradoxically, women did have better long-term survival in registry data, and this was hypothesized to be related to fewer cardiovascular comorbidities. We also found that women had less reported coronary artery disease.

A recent study demonstrates that women with CTEPH do have a greater need for postoperative medical therapy after PEA.[21] Residual or recurrent pulmonary hypertension has been reported to occur in around 1 in 4 patients after PEA.[24] Provided that anticoagulation has been therapeutic and that there has been no recurrent thromboembolism, this is generally thought to indicate the presence of microvascular disease that was not amenable to surgical resection. Previous work has demonstrated that segmental and subsegmental disease on CTPA is a risk factor for requiring medical therapy postoperatively.[13] Our study is the first to demonstrate that indeed men and women with surgical CTEPH do differ in presentation at the segmental and subsegmental vasculature and that the disease morphology and distribution are aligned with the clinical reports of greater microvascular disease in women. In this study, our CTPA slice thickness was generally 0.5 to 1.0 mm which is insufficient for imaging the microvasculature. Using the described imaging protocol, only 2 of the 144 included patients required preoperative diagnostic angiography to supplement CT at our center. Future studies could utilize photon counting CT to further interrogate the small vessels with higher spatial resolution.[25] Furthermore, a study of selective digital subtraction angiography in the segmental and subsegmental vasculature and its correlation with CTPA findings would be particularly valuable in assessing patients for balloon pulmonary angioplasty.

A Spanish cohort did demonstrate that women were more likely to undergo balloon pulmonary angioplasty, and this supports our finding that women have chronic thromboemboli that are fewer in number and more distal in the vasculature.[8] Presumably, patients were perceived as unresectable. Indeed, while the indication for balloon pulmonary angioplasty varies with user experience, at our center balloon pulmonary angiography is generally performed in patients with CTEPH who have disease in the segmental and subsegmental vasculature and are not PEA candidates. It should be noted though that at experienced centers, excellent results can be obtained surgically even in patients with predominantly segmental and subsegmental disease.[22,23] Other centers report much more broad use of balloon pulmonary angioplasty, particularly in Japan, even for treating lesions more proximal than the segmental vessels and the assessment of what treatment is preferred is made on a case-by-case level. Interestingly, the Japanese cohorts have a higher proportion of women, approaching 80%, and a higher proportion of disease in the distal vasculature which corroborates our findings of women presenting with a more distal phenotype.[26]

Our study has several limitations in addition to the single-center retrospective design. First, we only evaluated patients with surgical CTEPH and did not evaluate patients who were declined for surgery or patients in whom the pulmonary hypertension was potentially multifactorial, such as those who underwent synchronous cardiac surgery. By excluding nonoperated patients, we likely underestimate the proportion of distal disease and indeed, women are more likely to be treated medically and therefore we suspect that the difference between women and men in our study is underestimated. Second, our CT analysis was performed by our sole CTEPH program radiologist. While there is good reason to believe that the diagnosis of CTEPH requires a high degree of expertise and that less experienced readers make frequent errors in assessing this disease,[27] multicenter validation would be warranted. The scoring system used here has previously been evaluated for interobserver agreement and, as would be expected, agreement is strongest in the proximal vasculature and poor in the periphery, though agreement with the UCSD level is strong for all readers.[17] Finally, to identify subsegmental lesions, the parent segmental vessel must be patent and thus, in men where there is a predominance of segmental disease, the number of subsegmental lesions would be underestimated.

In conclusion, we found that there are sex-specific differences appreciable in CTPA of patients with CTEPH in chronic thromboembolism lesion type at the segmental and subsegmental levels. A higher prevalence of subsegmental disease and a lower burden of overall lesions in women, despite similar hemodynamics, may contribute to the reported disparity in surgical management.

CRediT authorship contribution statement

M.M., M.B., and G.G. contributed to conceptualization, methodology, data curation, and investigation. M.M., M.B., and K.L. contributed to formal analysis. L.D. and M.P. contributed to resources. All authors were involved in the writing, review, and editing of the manuscript. M.M. is the guarantor of the manuscript.

Disclosure statement

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhlto.2024.100130.

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