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Leiomyomas in an African Caribbean hysterectomy population considered to be ethnically related to African Americans.

Short title: Hysterectomy and leiomyomas in an African Caribbean Population.

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Abstract

Background: Uterine leiomyoma has been reported to be a worse problematic disease for African American than Caucasian women in the US. Data are almost non-existent for other populations of African ancestry. Our aim was to investigate the hypothesis of an equivalent influence of ethnicity on uterine leiomyomas for women of a French African-Caribbean population.

Basic procedures: Retrospective analysis of hysterectomies performed from 2010 to 2015 at the teaching hospital of Guadeloupe (French West Indies), where most inhabitants are of West African origin, was carried out. Data of the 899 hysterectomies, including those for malignancy, were collected, in particular, uterine weight.

Main findings: The indications were leiomyoma in 66.5% of cases and leiomyomas were found in 91% of all cases. The mean age and uterine weight were 51.7 years and 464 g for the entire population, 50.2 years and 488 g for the population without malignancies, and 47.0 years and 567 g for the population with leiomyomas.

Principal conclusions: The data were compared to those reported in the literature for several populations, notably African Americans and Caucasians in the US and mainland France. This comparison supports the hypothesis that Guadeloupean women, an African-Caribbean population, have characteristics in terms of uterine leiomyoma that are close to those of African Americans. Although confirmation is required, these results highlight the need for specific research, therapeutic approaches, and improved early management of these populations.

Key Words

African Caribbean, French West Indies, hysterectomy, uterine fibroid, uterine leiomyoma, uterine myoma.

Journal Pre-proof

Introduction

Uterine leiomyomas (ULMs) are the most common benign uterine tumors of women of child-bearing age [1]. ULM is the leading indication for hysterectomy in many countries, such as the USA [2] and France [3]. Its epidemiological indicators depend on the study population and how ULM is assessed [1]. As a consequence, the reported prevalence varies widely from 4.5 to 68.6% [1]. Among epidemiological indicators, ethnicity appears to be a major factor that should be considered to explain such wide variability for the prevalence of ULM in the general population. In the US, Asians, Hispanics, and Caucasians have been reported to have a similar prevalence of ULM [1,4]. In contrast, African American women have been reported to have higher rates of ULM than Caucasian women [4–6]. In addition, ULMs occur at an earlier age in the African-American population than in the US Caucasian population [4,5,7], are more numerous [5,7], are bigger (Weiss et al., 2009), more frequently symptomatic [5,7], and more often lead to hysterectomy [5,7] at a younger age [8], leading to a greater use of health resources [9]. Figures from the literature that illustrate the worst problematic impact of ULMs for African-American women relative to Caucasian women in the US are presented in Table 1. These tumors, only develop from menarche to menopause [6,10], highlighting the major role of steroid hormones in the physiopathology of ULM. However, the cause of ULM has not been clearly established. Ethnic factors appear to be important, but the respective roles of endogenous and extraneous components are not well defined. Reports addressing the role of ethnicity in the frequency of ULM are limited to the United States. The almost nonexistent literature for other populations of African ancestry, such as African-Europeans, Black Africans, African-Canadians, and African-Caribbeans represents an important knowledge gap [11].

In France, studies comparing groups defined by ethnicity are not allowed. Guadeloupe is a French overseas territory (French West Indies) for which it can be assumed that at least 80% of the 400,000 inhabitants are of African ancestry, as for the other Caribbean islands, which share a comparable history of slavery trade [12]. In addition, analyses of mitochondrial DNA have provided results on the African region of origin of populations of African ancestry living on the American continent. These results are in accordance with historical records on slavery trade [13]. Such analyses also support the idea that African-Caribbean populations share the same west sub-Saharan African ancestry as African Americans [13].

Hysterectomy is a leading surgical procedure for women of reproductive age in the United States [2] and mainland France [3,14]. There are several surgical approaches, which have become increasingly less invasive over the last two decades. The choice among the available approaches depends mostly on the size of the uterus, although several factors must be taken into account [15].

Here, the rate of ULM and the weight of uterus specimens from the hysterectomy procedures performed in our unit were assessed. These data were compared to those of literature reports to evaluate the hypothesis that the Guadeloupian population, mostly of African ancestry, is closer to the African-American population, in terms of ULM, than the French population, which is of mostly Caucasian ancestry.

Materials and methods

A retrospective study was conducted of hysterectomy procedures performed from 2010 to 2015 in the gynecological unit of the unique teaching hospital of Guadeloupe. Cases were

identified by manual research of operation room registries, in which all surgical acts are systematically recorded. All hysterectomy procedures were considered, regardless of the indication and surgical approach. The study was approved by the local IRB (A17_13_02_17_HYSTERECTOMIE).

The following data were recorded for all cases: patient age, hysterectomy indication (malignant disease i.e. all type of gynecological cancer requiring a HST as part of the treatment protocol, ULM, prolapse, or other), surgical approach (open laparotomy, laparoscopy (with or without a uterine artery ligation procedure and vaginal extraction) or vaginal (with or without wedge morcellation, coring, or bivalving)), uterine weight at histopathological examination of the fresh specimen, and at least whether ULM was found at histopathological examination of the uterus. A uterine weight > 300 g has often been proposed to define a “large uterus” and as the limit for hysterectomy performed by vaginal or laparoscopy approaches. Consequently, this weight was chosen as the cut-off in the analysis.

Continuous data (age and uterine weight) are expressed as the mean \pm standard deviation and extremes (ranges). Categorical data are expressed as the number and percentage [n (%)] by group.

Results

In total, 899 hysterectomy procedures were identified for the study period. The mean age was 51.7 ± 10.6 years (25 - 97) for the entire population and 50.2 ± 9.4 years (25.5 - 97) if malignancies were excluded. The mean age by indication was 61.6 ± 12.3 years (34 - 89) for

malignancies, 47.0 ± 4.2 years (32 - 65) for ULM, 65.7 ± 11.4 years (40 - 89) for prolapse, and 54.7 ± 13.4 years (25 - 97) for other causes.

The indications were malignant disease [117 (13.0%)], ULM [598 (66.5%)], prolapse [96 (10.7%)], and other causes [88 (9.8%)]. For the latter group, the indications were postpartum hemorrhage, endometriosis, adenomyosis, endometrial hyperplasia, relapse of postmenopausal bleeding, and adnexal pathology. At least one ULM was found for 766 (85.2%) uteruses at pathological examination of all hysterectomies and for 712 (91%) if malignancies were excluded. If hysterectomies for ULM were excluded, a ULM was found for 171 (56.8%) uteruses of the remaining indications. The distribution of indications between malignant diseases, ULM, prolapse, and other causes for each surgical approach were 11.8, 77.7, 1.2, and 9.3% for open laparotomy, 19.5, 65.2, 3.8, and 11.5% for laparoscopy, and 3.2, 26.8, 62.2, and 7.9% for vaginal, respectively.

The surgical approaches used were open laparotomy [485 (54%)], laparoscopy [287 (32%)], and vaginal [127 (14%)]. In our study, a uterus of < 300 g represented the 75th percentile of uteruses removed by laparoscopy. For this population of patients [482 (53.6%)] the surgical approaches used were open laparotomy [159 (33.0%)], laparoscopy [210 (43.6%)], and vaginal [113 (23.4%)].

The uterine weights for all 877 cases (22 missing weights), each indication group, and each surgical approach group are presented in Table 2. The distribution of uterine weight is presented for all 877 cases in Figure 1a and according to indication in Figure 1b and surgical approach in Figure 1c.

Comment

These descriptive results of hysterectomy procedures, focusing on ULM, support the hypothesis that the Guadeloupien African-Caribbean population is closer to the African-American population than that of mainland France, which is mostly Caucasian. Our results also highlight the rate of ULM in the hysterectomy procedure and the high weight of the uteruses removed in this population of African descent.

Our results for patient age and uterine weight were compared to equivalent results of studies performed in the United States, mainland France, and Asia (Table 3). Uterine weights for our study population were closer to those of African Americans than those of Caucasians in the US, Caucasians in France, or Asians.

Previous reports comparing African-American to Caucasian populations found that ULM is a worse problematic disease for African-American women at a younger age (Table 1). Our results concerning age at hysterectomy for the entire study population, with or without inclusion of malignancies, did not confirm this finding following comparison with other selected studies (Table 3). This may be explained by our strategy, which included all hysterectomy indications, with no exclusion of malignancies or prolapses. However, the mean age of our population was largely unaffected when malignancies were excluded (Table 3). Another possibility may be the impact of the French social medical system on the medical history of patients with ULM. Guadeloupe has almost free access to medical and surgical care, as does Mainland France. The possibility that our patients had a longer history of health care for ULM than African-American women cannot be excluded.

The uterine weight, and thus size, in our population (Figure 1) was clearly higher than that of hysterectomy procedures reported for US Caucasian, mainland French, and Asian women (Table 3). One study conducted in the Parisian region reported a higher average uterine weight than in the other studies [15]. However, it has been shown that the Caribbean and African communities are larger in the Parisian region than in other regions of mainland France [16,17]. The possibility that such a larger proportion of women of the Caribbean and African communities is responsible for the higher reported uterine weights from hysterectomies in the Parisian region study cannot be excluded.

More than half of our hysterectomy procedures were performed by laparotomy (Figure 1c). This is a high rate, given the tendency and recommendations to use less invasive approaches. However, this result may be explained by the inclusion of malignancies in our study, which are more likely to be treated by open laparotomy than benign diseases, despite recommendations for mini-invasive surgery. Furthermore, the high weight, and thus large size, of the uteruses in our study may have also led to such a high rate of open laparotomies (Figure 1b, 1c). The influence of uterine size on surgical approaches has been previously reported [2,15]. This is corroborated by analysis of the subpopulation with a uterus smaller than 300 g, corresponding to the 75th percentile of hysterectomies performed by laparoscopy. Only one third of the hysterectomy procedures in this population were by laparotomy. Our findings support that uterine weight is a major factor that affects the choice between laparotomy and less invasive surgical approaches for hysterectomy. However, laparoscopic [18] and vaginal [19] surgical approaches can be performed on patients with a large uterus (> 280 - 300 g) with a ULM. In such cases, several factors must be considered, including the surgeon's experience [19,20].

However, open laparotomy is almost unavoidable for a very large uterus (> 500 – 1000 g) with a ULM [21].

Most studies on the characteristics of hysterectomy exclude malignancy. This exclusion is justified by study objectives that tailor the methods for assessing the surgical approaches or epidemiology of hysterectomy. Malignancy indications were not excluded in our study, which aimed to assess the rate of ULM for the broadest population possible (Figure 1b). Thus, our findings show that hysterectomy was indicated for ULM in 66.5% of cases but was also found in 56.8% of hysterectomies for other indications, including malignancy, resulting in ULMs being found in 85.2% of all hysterectomies. This finding is informative, as ULM, due to the larger size of the uterus, may be an additional factor that influences the treatment strategy, especially the choice of the surgical approach in other hysterectomies for which ULM is not the indication.

Our methodology was based solely on a comparison of descriptive data with that in the literature, without any statistical tests. Consequently, our conclusions concerning ULM must only be taken as simple but convincing arguments to support the hypothesis that Guadeloupien women, considered as an African-Caribbean population, may share the epidemiological characteristics reported in the US for African-American women. However, this evidence cannot be considered to have a high standard of scientific strength. Another limitation is the monocentric design of this study. In addition, this center is the referral unit for gynecological surgery and the only teaching hospital in Guadeloupe. Thus, a recruitment bias cannot be excluded, as treatment of the more complicated and advanced cases in Guadeloupe would have been included, including ULMs, with a subsequent overestimation of the rate of ULM and the uterine weight in our general population. Thus, our results cannot be

taken as a rigorous assessment of the epidemiological indicators of ULM in the Guadeloupian population. Indeed, this was not among our study objectives. However, a previous study, based on a population strategy assessment, confirmed the tendency found by studies of hysterectomy populations of a higher rate of symptomatic ULMs at a younger age for African American than Caucasian women [5]. In addition, the cumulative incidence of ULM has been assessed by pelvic ultrasound screening of a randomly selected sample of women in the US [5]. In this study, more than 80% of African-American and nearly 70% of Caucasian women had ULM. Thus, the rate of ULM found in the entire population in our study (82%) is similar to that of this assessment in the African-American population. Such a comparable rate of ULM supports the influence of ethnic factors in the onset and development of ULM, given the possibility of shared west sub-Saharan African ancestry between African-American and Caribbean populations [13]. It would have been interesting to include sub-Saharan population studies in our comparison (Table 3). However, we did not find such reports in our literature research.

Conclusion

Despite certain limitations related to the weakness of the study protocol, requiring future confirmation studies, our results on the rate of ULM in the hysterectomy patient population can be considered to reflect ULM in the general Guadeloupian female population. Our results are in concordance with those reported for ethnic comparisons in the US, providing further support to the hypothesis of an ethnic component in the onset of ULM, as African Americans and African Caribbeans share the same west sub-Saharan genetic background. Thus, our

results suggest that specific attention should be given to such populations in which ULM appears to have a greater impact on health. Such attention could be in the form of both therapy and research, possibly leading to new medical treatment strategies and early care.

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Conflict of interest

P. Kadhel receives grants and personal fees for consulting activities from Gedeon Richter, France. None of the other authors reports a conflict of interest.

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Figure legend

Distribution of uterine weights by percentage for all cases (A), by indication (B), by surgical approach (C).

A: 877 hysterectomies (weight missing in 22 cases)

B: distribution of weight by indication (malignancy, myoma, prolapsed, other)

C: distribution of weight by surgical approach (open laparotomy, laparoscopy, vaginal)

Figure 1: Distribution in percentages of uterus weight for all cases (a), according to the indication (b) and according to the surgical approach (c).

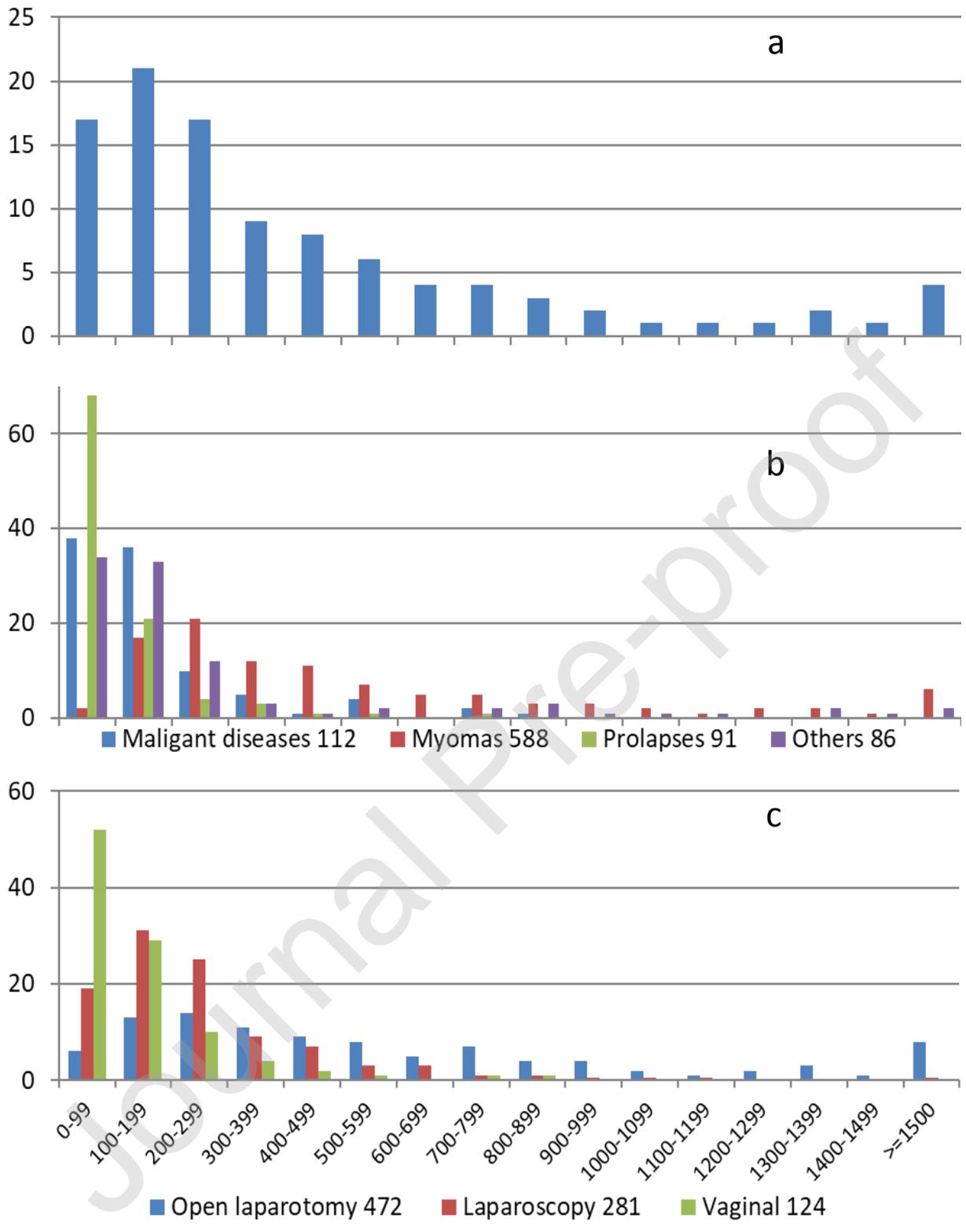


Table 1. Figures from the literature that illustrate the higher impact of uterine leiomyomas (ULM) on the health of African Americans relative to that of Caucasians in the United States.

	African American	Caucasian	p
Higher rates			
Odds ratio of the age-specific cumulative incidence (35-49 years) [5]	2.9 (95% CI, 2.5-3.4)	1	< 0.001
Age standardized rate [4]	30.6/1,000	8.9/1,000	
Relative risk from review [1]	2.14 to 3.25	1	
Diagnosis at younger age			
Mean age at diagnosis in a random population sample [5]	33	36	< 0.001
Mean age at diagnosis in a hysterectomy patient population [7]	37.5 ± 7.9	41.6 ± 6.6	< 0.001
More numerous			
Percentage of multiple focal ULMs [5]	73	45	
Number of ULMs (distribution in %) [7]			< 0.001
1-2	18	39	
3-6	26	42	
>7	56	36	
Bigger			
Uterine weight of hysterectomy with ULMs (g), median [IQR] [8]	448 [272–794]	240 [142–440]	< 0.001
More frequently symptomatic			
Clinically relevant ULM in % [5]			

Women from 35 to 39	30 to 40	10 to 15	
Women in their late 40s	50	35	
Odds ratio	2.6 (95% CI, 2.2-3.0)	1	< 0.001
Symptoms in a hysterectomy patient population in % [7]			
Amenia	59	38	< 0.001
Severe or very severe pelvic pain	59	41	< 0.001
Constipation	21	13	= 0.017
Higher frequency of hysterectomies			
Percentage of hysterectomies in random population sample [5]	14	7	
Younger age at hysterectomy			
Mean age at hysterectomy in year [8]	48.0 ± 3.0	50.0 ± 3.3	< 0.001
Greater use of health resources			
Cost to treat in US \$ per 10,000 [9]			
Hysterectomy	2,607,006	1,198,930	
Outpatient clinical	228,975	64,387	

Table 2. Weight of the 889 uteruses after hysterectomy.

Subgroup	Number	Mean (g)	Minimum (g)	Maximum (g)
Whole population	877 ^a	464	20	10,000
Malignancies excluded	765 ^a	488	22	6,439
By hysterectomy indication				
Malignancies	112	296	20	10,000
Uterus Leiomyomas	588	567	43	6,439
Prolapses	91	109	22	796
Others	86	351	38	6,000
By surgical approach				
Open laparotomy	472	676	20	10,000
Laparoscopy	281	250	22	2,188
Vaginal	124	137	24	856

^adata missing for 22 patients of the entire study population and 17 when excluding malignancies

Table 3. Comparison of uterine weight after hysterectomy.

Study	Study Period	Population	Number (n)	Mean age (years)	ULM (%)	Uterine weight (g)	
						All	[Surgical approach]
Our study, Guadeloupe	2010 - 15	African Caribbean	899	51.7	66.5	464	[676 – 250 – 137] ^a
Our study, Guadeloupe ^b	2010 - 15	African Caribbean	782	50.2	91	488	[699 – 280 – 138] ^a
Studies in the US							
Kjerulff <i>et al.</i> [7]	-	Caucasian ^b	836	44.6	59	319	
	-	African American ^b	409	41.7	89	421	
Weiss <i>et al.</i> [8]	1995 - 97	Caucasian ^b	64	50	63	240	
		African American ^b	61	48	85	448	

Studies in Mainland France

Martin <i>et al.</i> [22]	1992 - 96	Caucasian (Lyon (city)) ^b	682	50.3	[349 – 185 – 137] ^a
Levêque <i>et al.</i> [23]	1997	Caucasian (Brittany (region)) ^c	340	47	309 and 362 for ULM only
Debodinace <i>et al.</i> [14]	1997	Caucasian (North (region)) ^b	423	48.3	[579 – 281 – 245] ^a
Boukerrou <i>et al.</i> [24]	1996 - 98	Caucasian (Lille (city)) ^b	453	46.5	[612 – 209 – 258] ^a
David-Montefiore <i>et al.</i> [15]	2004	Mixed (Parisian region) ^a	634	51.4	[723 – 280/230 ^d – 226] ^a

Studies in Asia

Leung <i>et al.</i> [25]	2002	Asian (Hong Kong)	950	320	[427 – 125 – 150] ^a
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ULM: leiomyomas

^a(open laparotomy – laparoscopy – vaginal), ^bhysterectomies for malignancies were excluded, ^chysterectomies before 60 for benign indications, ^dlaparoscopically performed/assisted.