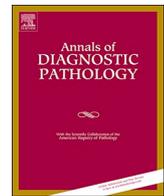




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Original Contribution

Benign breast conditions: An eight-year single-centre histopathological review of women presenting with mass lesions at the Korle-Bu Teaching Hospital, Ghana

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1. Introduction

In recent times, although there has been heightened breast cancer awareness among African women, there is still a great challenge in breast care seeking behaviour among such population with most presenting late [1]. Physicians, oncologists, surgeons and pathologists are confronted on daily basis with onus of deciphering between a trivial benign lesion and a more life-threatening invasive carcinoma of the breast. This has an immense influence on the decision-making process regarding the prognosis, treatment and the quality of life of patients presenting with breast lumps. Especially in resource limited settings as pertains in most less developed and developing countries, the importance of clinicians making informed evidence-based decisions on the differential diagnosis of breast lumps in situ cannot be overemphasised.

Benign breast conditions consist of heterogeneous spectrum of histologic subtypes involving non-proliferative breast lesions, proliferative breast lesions without atypia, and proliferative breast lesions with atypia [2-5]. Research has shown that benign breast tumours make up about 90% of all clinical presentations with fibroadenoma and fibrocystic change being the most frequently occurring [6,7]. There is further evidence that fibroadenoma is most prevalent in dark skinned populations [8].

Although benign breast conditions may appear trivial, presence of some benign breast lump puts a patient at an increased risk of developing breast cancer [9,10]. Compelling evidences indicate certain histological subtypes such as atypical ductal and atypical lobular hyperplasia have increased risk of subsequent breast cancers [3,11,12]. According to Dupont and colleagues, atypical lobular hyperplasia increases cancer risk by 3 folds [13] while a 4 to 5 fold increase has been found associated with atypical ductal hyperplasia [3]. Racial disparities have been found to exist in both incidence and survival. African American women are at significantly greater risk of developing early-

onset breast cancer (< 35 years at diagnosis) and have poorer survival when compared with Caucasian women [14-16]. This disparity may be attributed to factors such as an increased body mass index (BMI), higher rates of obesity, higher parity, earlier age at first birth, and lower rates of breast feeding in these African American women compared with their Caucasian counterparts [15]. Although this information is well documented in African American women with same African decent as African women, it may not be entirely true with the later. Other risks factors such as family history of cancer, alcohol consumption, smoking, and hormone replacement therapy have been identified as well as some environmental and genetic factors [17].

Very little is known about the spectrum of histologic subtypes of benign breast lesions in Ghana, their geographical pattern of occurrence and their relative cancer risks. It is therefore crucial that oncologists, pathologists, radiologists and surgeons not only decipher benign breast conditions from breast cancer but also have in-depth knowledge about the geographical pattern of occurrence of these disorders in Ghana. Benign breast lesions and their cancer risks have extensively been studied in Caucasian populations but very limited information exists in African populations. The cancer risk estimate of benign breast lesions in Sub-Saharan Africa remains largely unknown and due to the differences in genetic and environmental factors among populations, results from studies carried out on Western or other Caucasian populations cannot entirely be extrapolated to the African population. It is therefore necessary that the spectrum of benign breast conditions (BBC) and their genetic and environmental basis are thoroughly studied among African populations because of its high prevalence in women, impact on the quality of life and their risk of becoming cancerous in some histological subtypes. Better understanding of the risk factors for BBC, especially the relation between BBC and known risk factors for breast cancer, will help to clarify the relation between BBC and breast cancer and increase understanding of the carcinogenic process in this population.

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The aim of this study is to determine the relative frequencies of the various benign breast conditions among patients who attended the Korle-Bu Teaching Hospital, Accra, Ghana between 2006 and 2013 as well as determine the various demographic characteristics influencing the type of BBC a patient presents and compare various parameters statistically.

2. Methodology

Korle-Bu Teaching Hospital is the premier tertiary health care facility in Ghana located in the Greater Accra Region of Ghana. It is a 2000 bed capacity facility with 17 clinical and diagnostic departments/units with an estimated daily attendance of 1500 patients and 250 patient admissions [18]. It serves as the main referral centre for the entire southern Ghana and beyond [18].

All data were collected from the Department of Pathology with average yearly histopathology case load between 5000 and 8000. This Department, the largest in Ghana, receives surgical specimens from the Korle-Bu Teaching Hospital, the largest referral hospital in Ghana. The Department also receives specimens from other health facilities within the Accra metropolis, the Greater Accra Region, and the 4 other southern regions of Ghana: Central, Western, Eastern, and Volta regions [18]. Although these are data obtained from a single-institution, the sample size is adequate and largely representative of benign breast conditions as seen in Ghana. This will allow for evaluation of the clinical and histologic characteristics of Ghanaian women diagnosed with benign breast conditions.

This retrospective study included breast biopsy (tru-cut, excision, and core) reports of all patients presenting with breast lumps between January 2006 and December 2013 at the Korle-Bu Teaching Hospital, Accra, Ghana. Clinical and demographic data regarding age, gender, and clinical information were obtained from the histopathology request forms and registry. The study analysed basic demographical and pathological information.

Comparison between the parameters was done using IBM Statistical Package for Social Sciences Software v 24 (SPSS Inc.: Chicago, IL, USA) and Microsoft Excel 2010 for Windows and checked for range and internal consistency before analysis using the same packages, and *p* value calculation performed at α level. Literature search was performed utilizing the Google search engine (<https://www.google.com/>), National institute of Health, PUBMED.gov website (<http://www.ncbi.nlm.nih.gov/pubmed>).

3. Results

During the eight-year period, a total of 2805 patients within the age range of 1 and 86 (mean 26.99 ± 11.03 years) presented with various forms of benign breast conditions (BBC). Table 1 shows the descriptive statistics of the demographic features of the lumps of patients with BBC. 85.0% of the patients were below the age of 40 (the younger age group) with a mean age of 23.19 ± 5.98 years while 15.0% were aged above 40 years (Older age group) with a mean age of 48.5 ± 7.9 years (Table 1). The modal age range was 20–24 (29.6%) (Fig. 1 and Table 2). 1194 (46.8%) patients had Right breast lumps, 1152 (45.8%) patients

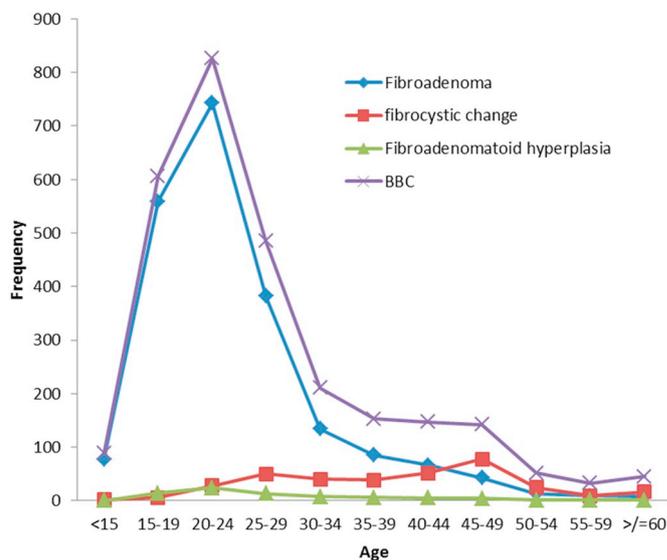


Fig. 1. The relative frequencies of the most common benign breast conditions with age.

Table 2 Age distribution of patients with benign breast conditions.

Age in years	Frequency	Percentage
< 15	88	3.2
15–19	606	21.7
20–24	827	29.6
25–29	485	17.4
30–34	212	7.6
35–39	153	5.5
40–44	147	5.3
45–49	142	5.1
50–54	52	1.9
55–59	33	1.2
> / =60	45	1.6
Total	2790	100

had left breast lumps and 203 (8%) patients had bilateral breast lumps. There was therefore statistically no significant difference in the site of the lump between the older and the younger age groups (*p*-0.663). Patients therefore predominantly presented with unilateral as opposed to bilateral masses (*p*-0.000) (Table 5) but of the unilateral masses there was no significant difference between the occurrences of lumps in either the left or right breast (*p*-0.386). 77.7% were solitary masses while 22.3% were multiple. The presence of multiple lumps makes it most likely to be involving both breasts (*p*-0.000). The size of the masses in the widest diameter ranged from 0.2 to 32 cm (mean 3.72 ± 2.73 cm) (Table 1). The mean size of mass in the younger age group was 3.6 ± 4.39 and 4.3 ± 5.79 in the older age group. A significant age specific association therefore exists between increasing size of the mass and increasing age (*p*-0.000). The weight of the masses ranged between 0.9 and 1500 g (mean 70.34 ± 179.15 g) (Table 1). There was an age

Table 1 Descriptive statistics.

	N	Mean	Std. Error	Std. Deviation	Variance
Age	2790	26.99	0.209	11.036	121.786
Younger age group (< 40 years)	2372	23.19	0.123	5.986	35.836
Older age group (≥ 40 years)	418	48.53	0.390	7.982	63.708
Size of mass (cm in largest diameter)	2704	3.7240	0.053	2.734	7.476
Size of mass (< 40 years)	390	4.43	0.293	5.79	33.52
Size of mass (≥ 40 years)	2301	3.60	0.075	4.39	19.29
Weight of mass (g)	245	70.35	11.446	179.158	3.210E4

Table 3
Frequency of benign breast conditions.

Benign breast condition	Frequency	Percent	Mean age in years
Fibroadenoma	2130	76.0	24.0 ± 8.3
Fibroadenomatoid changes/ hyperplasia	78	2.8	28.0 ± 10.7
Fibrocystic change	347	12.4	39.3 ± 11.7
Benign Phyllodes tumour	41	1.5	38.0 ± 14.2
Intraductal papilloma	38	1.4	45.4 ± 8.3
Granular cell tumour	5	0.2	24.6 ± 17.2
Lactating adenoma	25	0.9	29.6 ± 6.0
Tubular adenoma	60	2.1	22.7 ± 15.0
Lymphocytic mastitis	11	0.4	31.2 ± 8.8
Granulomatous mastitis	6	0.2	35.0 ± 10.2
Chronic mastitis	37	1.3	42.0 ± 12.5
Atypical hyperplasia	4	0.2	48.3 ± 6.1
Ductal hyperplasia	12	0.4	43.4 ± 13.8
Microglandular hyperplasia	1	0.0	45.0 ± 0.0
Stromal hyperplasia	2	0.1	12.0 ± 1.0
Fibroepithelial polyp	3	0.1	24.3 ± 2.1
Fibrolipoma	1	0.0	29.0 ± 0.0
Total	2805		100

specific association between the young (Below 40 years) and the older (above 40 years) and the benign breast condition they presented with ($p < 0.000$). Table 2 shows the age distribution of BBC of patients.

The commonest benign breast condition was Fibroadenoma (76%) (Table 3) occurring mostly in patients below 40 years (93.4%) with a predominant right breast preference over the left (77.1% vs 73.3%; $p = 0.038$). The Age range of patients with fibroadenoma was between 1 and 82 (mean 24.02 ± 8.3 years) (Table 3). Fibroadenoma consistently had the highest yearly prevalence over the eight-year period under study (Fig. 1). The second most common lesion was fibrocystic change (12.4%), commoner in the older age group (43% vs 7%; $p = 0.000$). This was followed by fibroadenomatoid changes/hyperplasia and tubular adenoma with 2.8% and 2.1% respectively.

From Table 4, the following conditions were also predominant in the older age group: Benign Phyllodes tumour (5% vs 0.8%; $p < 0.000$), Intraductal papilloma (6.4% vs 0.4%; $p < 0.000$), and Ductal hyperplasia (1.4% vs 0.2%; $p < 0.001$). For the younger age group, Tubular adenoma (2.4% vs 0.5% $p < 0.013$), Atypical hyperplasia (0.7% vs 0%; $p < 0.000$) were predominant. There was statistically no significant difference between the groups with respect to Fibroadenomatoid change/

Table 4
Age specific distribution of benign breast conditions.

Benign breast condition	Age specific segregation (%)			p-Value
	≥ 40	< 40	Total	
Fibroadenoma	139(33)	1981(84)	2120(76)	0.000
Fibroadenomatoid changes/ hyperplasia	13(3)	65(2.4)	78(2.8)	0.658
Fibrocystic change	181(43)	165(7)	346(12.4)	0.000
Benign Phyllodes tumour	21(5)	20(0.8)	41(1.5)	0.000
Intraductal papilloma	27(6.4)	11(0.5)	38(1.4)	0.000
Fibroepithelial polyp	0(0)	3(0.1)	3(0.1)	0.466
Atypical hyperplasia	3(0.7)	0(0)	3(0.1)	0.000
Ductal hyperplasia	6(1.4)	6(0.3)	12(0.4)	0.001
Lactating adenoma	2(0.5)	23(1)	25(0.9)	0.322
Granular cell tumour	0(0)	5(0.2)	5(0.2)	0.346
Tubular adenoma	2(0.5)	56(2.4)	58(2)	0.013
Lymphocytic mastitis	1(0.2)	10(0.4)	11(0.4)	0.580
Granulomatous mastitis	1(0.2)	5(0.2)	6(0.2)	0.912
Chronic mastitis	21(5)	15(0.6)	36(1.3)	0.000
Epithelial hyperplasia	2(0.5)	1(0.0)	3(0.1)	0.012
Microglandular adenosis	1(0.2)	0(0.0)	1(0.0)	0.017
Fibrolipoma	0(0)	1(0.0)	1(0.0)	0.674
Stromal hyperplasia	0(0)	2(0.1)	2(0.1)	0.552
Total	420	2369	2789	

Table 5
Linear and multivariate regression analysis of factors influencing the benign breast conditions.

Factor	Benign breast condition		
	Beta	SE	p-Value
Age	0.278	0.004	0.000
Site	-0.015	0.080	0.462
Size	0.079	0.050	0.000
Weight	0.001	0.001	0.240
Numeracy	0.033	0.117	0.083
Multivariate analysis of factors influencing the benign breast conditions			
Age	0.255	0.004	0.000
Size	0.065	0.016	0.001

hyperplasia (3% vs 2.7%; $p < 0.685$), Granular cell tumour (0.2% vs 0%; $p < 0.346$) and Lactating Adenoma (0.4% vs 0.9%; $p < 0.322$). Benign Phyllodes tumour was the only breast condition aside fibroadenoma that had a significant association with the site of the mass with a common occurrence in the left breast (2.4% vs 0.9%; $p = 0.004$). With the inflammatory lesions, chronic mastitis was predominant and more prevalent in the older age group (5% vs 0.6%; $p < 0.000$), whereas lymphocytic and granulomatous mastitis had no significant difference between the age groups.

To assess factors associated with the histological type of benign breast condition a patient presents with, bivariate and multivariate regression models were developed (Table 5). Linear regression analyses showed that the independent factors that influenced the type of benign breast condition a patient presents which include, Age of the patient ($p < 0.000$), and size of the mass ($p = 0.000$) but not the site of the lump (left, right or bilateral), and the number of lumps (single or multiple) and the weight of the mass. A multivariate analysis also indicated the Age ($p < 0.000$) and increasing size ($p < 0.001$) of the mass were factors that influenced the type of benign breast condition a patient present with (Table 5).

4. Discussion

The increasing level of breast cancer awareness coupled with the anxiety and fear surrounding its prognosis have significantly increased the health seeking behaviour of African women with breasts lumps. Elsewhere, research has revealed an association between some Benign Breast Conditions and an increased risk for developing a subsequent breast cancer [5,19]. Limited research however exists among African women regarding BBCs and their associated cancer risks. Regardless of the breast lesions, it is important for clinicians and surgeons to be able to distinguish benign breast lesions from malignant ones and also differentiate between the trivial and the not-so-trivial ones. An understanding of the spectrum of benign breast changes in African women is necessary to optimize diagnosis and treatment aimed at improving quality of life.

In this study of women presenting with mass lesions at the Korle Bu Teaching Hospital, Ghana, benign breast conditions occurred in all age groups with peak prevalence between 20 and 24 years (Fig. 1). The mean age of presentation of BBC in this study was 27 years with most of the cases occurring before the age of 40 years in keeping with Olu-Eddo and Ugiagbe's study in Nigeria [20] and Albasri's study in Saudi Arabia [21]. The association between age and breast cancer risk has been studied in several contexts and the importance of such association cannot be overemphasised [5,11,22,23]. This study revealed a high prevalence of benign breast lesions among the younger age group giving the direct indication of an anticipation of increased breast cancer risks in about a decade or two within the population [5]. The younger age group (< 40 years) had larger lump size which may be attributable to the greater hormonal influence on the breast tissue stimulating cell

proliferation [6] (Table 1). About 3 out of 4 patients presenting with BBC had single masses but those with multiple lumps are more likely to have it in both breasts. Multiplicity of BBC according to Worsham et al. is associated with increased risk of breast cancer [22].

Consistent with previous studies [20,21,24–28], the lobular stromal lesion fibroadenoma was the most common BBC in this study representing 76% of all benign lesions within the 8 year period. This figure is similar to findings from studies conducted in Ghana and Nigeria which reported prevalence of 70% [24] and 72.5% [20] respectively but higher than other studies reporting prevalence of 44%, and 45.6% in Nigeria [28,29], 42% in Sudan [30], 44.3% in Saudi Arabia [21] and 39.4% in Jamaica [27]. This high prevalence is reported in dark skinned populations [8,31] and may be attributed to increased incidence in underlying and acquired genetic changes such as loss of heterozygosity (LOH) and microsatellite instability [32,33]. BRCA1/2 mutation is also known to be associated with increased frequency of benign or malignant breast lesions [34]. Social and environmental factors such as parity, hormone replacement therapy, breast feeding, smoking and heightened consumption of vitamin C may also be among the contributing factors for the observed disparity though inconclusive due to conflicting reports from previous studies [17,24].

Furthermore, fibroadenoma was found to be predominant in the younger age group with the mean age at presentation as 24 years and a peak of prevalence occurring within the 20–24 age group in keeping with Anyikam et al. [28], and Worsham et al. [35]. It is not surprising to find fibroadenomas in this age group since it is about the period when lobular structures are added to the ductal system. Unilateral fibroadenomas were predominant in this study with a significant right breast preference; the reason for this is unknown.

The second most common BBC was fibrocystic change accounting for 12.4% of all women presenting with breast masses, occurring mostly in the third and fourth decade of life (Table 6) with a mean age of 39.3 years, a figure consistent with findings from studies by Uwaezuoke and Udoye [33] and Albasri [40]. Figures higher than the observed have been recorded in other studies in Nigeria with prevalence of 23.8% [20], 22.9% [28] and 27.7% [36]. The reason for such disparity is unknown. However, studies conducted in Italy and USA had fibrocystic change as the most common BBC [37]. Previous studies have indicated that fibrocystic changes do not incur any increased risk of breast cancer generally [6] however proliferative elements with atypical cellular changes confers and increased risk [38–40].

In this present study, tubular adenoma accounted for about 2.1% of

all the benign breast conditions occurring mostly in the younger age group in concordance with Sengupta et al.'s study [41] but slightly higher than the maximum incidence of 1.7% reported by other studies [42–45]. Although tubular adenoma usually presents in patients of child bearing age, this study and other previous studies have shown that it is a differential to consider for a gradually enlarging breast mass in a postmenopausal woman [42]. Lactational adenoma also represented 0.9% of BBC. Although breast adenomas are rare and benign, there have been reports of cases where infiltrating carcinoma has been associated with lactational adenoma [45].

Benign phyllodes tumours, one of the rare breast tumours accounted for 1.5% of the BCC with a mean age of 38.0 years. This is lower when compared with other studies with an average age of 40 to 50 years [46–48]. Although this tumour type usually occurs in the older age group in previous studies, this study observed its occurrence in all age groups with a higher prevalence in the older age group ($p = 0.000$) in keeping with previous reports. Surprisingly, the study recorded two cases of benign phyllodes tumour in patients below 15 years [49].

The histological assessment of risk of developing invasive breast cancer is currently based on conventional morphological criteria. This outlines a morphological spectrum of epithelial proliferative lesions with different levels of risk of developing invasive breast cancer [50]. At the beginning of the spectrum lies usual ductal hyperplasia conferring about a 1.5-fold increased risk of breast cancer. To the other extreme end is Ductal Carcinoma In Situ (DCIS) with an 8 to 10 fold increased risk. In between these extremes lies Atypical Ductal hyperplasia (ADH) with a 4–5-fold increase which may even be greater in premenopausal women [9,51]. ADH occupies a transitional zone between benign and malignant disease and possesses some characteristic cellular features of invasive disease. Its premalignant status gives it clinicopathological significance [52]. This study revealed a lower prevalence of atypical ductal hyperplasia (0.2%). This is likely due to the fact that only patients who had mass lesions and presented to the hospital were studied. It has been reported that most ADHs do not present as mass lesions and thus would not be part of our study population. A study in Saudi Arabia reviewing cases in the same 8-year period as this current study, on the other hand, did not record any of these histologic subtypes [21]. Conversely, a study in Nigeria with comparable total number of sample size as this current study indicated a relatively increased prevalence of 3.6% of atypical ductal hyperplasia [20]. The current study also revealed a predominant occurrence of both atypical hyperplasia and ductal hyperplasia in the older age group

Table 6
Age distribution of benign breast conditions.

Benign breast condition	Age in years											Total
	< 15	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	> / =60	
Fibroadenoma	78	559	743	382	134	85	66	43	13	9	8	2120
Fibroadenomatoid changes/hyperplasia	0	14	24	13	8	6	5	4	1	1	1	77
Fibrocystic change	2	6	28	50	40	39	52	78	25	9	17	346
Benign Phyllodes tumour	2	3	3	3	7	2	6	4	3	5	3	41
Intraductal papilloma	0	1	2	5	0	3	5	7	5	4	6	38
Fibroepithelial polyp	0	0	1	2	0	0	0	0	0	0	0	3
Atypical hyperplasia	0	0	0	0	0	0	1	1	0	1	0	3
Ductal hyperplasia	0	0	0	2	0	4	3	0	0	0	3	12
Stromal hyperplasia	2	0	0	0	0	0	0	0	0	0	0	2
Microglandular adenosis	0	0	0	0	0	0	0	1	0	0	0	1
Epithelial hyperplasia	0	0	0	0	1	0	0	0	0	1	1	3
Granular cell tumour	0	2	1	1	0	1	0	0	0	0	0	5
Lactating adenoma	0	2	1	10	7	3	2	0	0	0	0	25
Tubular adenoma	3	16	23	9	3	2	1	0	0	0	1	58
Lymphocytic mastitis	0	2	0	2	4	2	0	0	1	0	0	11
Granulomatous mastitis	0	0	0	2	2	1	0	0	0	1	0	6
Chronic mastitis	1	1	0	3	5	5	6	4	4	2	5	36
Fibrolipoma	0	0	0	1	0	0	0	0	0	0	0	1
Total	88	606	826	485	211	153	147	142	52	33	45	2788

(≥ 40 years) ($p = 0.000$ and 0.001 respectively).

In Table 5, this study shows age and size of the mass as the only two demographic parameters that independently associate with the type of BBC a patient presents with. This is further buttressed with the fact that certain BBCs are predominant in certain age brackets. For instance, Fibroadenoma is predominant in the younger age group. It is also evident that certain BCCs also present bigger tumour sizes than others. This implies that age of the patient and size of the mass are the two most important parameters to consider in decision making by physicians surgeons before definitive diagnosis is arrived at by pathological analysis.

5. Conclusion

There is little variation in the clinicopathological and demographic characteristics of BBC occurring in Ghanaian women and those reported in existing literature from outside Ghana. Fibroadenoma is the most prevalent BBC in Ghana. A high prevalence of BBC was found among the younger age groups. Age and increasing size of mass are the two most important parameters associated with the type BBC in Ghanaian women. This study confirms the disparity in the prevalence of fibroadenoma between Africans than Caucasians and the fact that the prevalence is higher in the former. Further research is required to ascertain the exact reasons for this disparity.

Fibrocystic change was the second highest BBC patients presented with, affecting patients above 40 years of age. This study revealed relatively lower rates of atypical epithelial hyperplasia with the few reported occurring in patients above 40 years. This may be due to the absence of breast cancer screening with subsequent late presentation of patients. It is essential that screening programs targeting such lesions are intensified to help in early detection of premalignant and malignant lesions. This will lead to better surveillance, earlier diagnosis, and ultimately, improved survival.

Ethical consideration

This article does not contain any studies with human participants or animals performed by any of the authors. Archival blocks and patients' registry were used with no contact with human participants.

Declaration of Competing Interest

All authors declare that they have no conflict of interest.

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