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Is clinical breast examination important for breast cancer detection?

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ABSTRACT

Background Screening clinical breast examination (CBE) is controversial; the use of CBE is declining not only as a screening tool, but also as a diagnostic tool. In the present study, we aimed to assess the value of CBE in breast cancer detection in a tertiary care centre for breast diseases.

Methods This retrospective study of all breast cancers diagnosed between July 1999 and December 2010 at our centre categorized cases according to the mean of detection (CBE, mammography, or both). A CBE was considered "abnormal" in the presence of a mass, nipple discharge, skin or nipple retraction, edema, erythema, peau d'orange, or ulcers.

Results During the study period, a complete dataset was available for 6333 treated primary breast cancers. Cancer types were ductal carcinoma *in situ* (15.3%), invasive ductal carcinoma (75.7%), invasive lobular carcinoma (9.0%), or others (2.2%). Of the 6333 cancers, 36.5% (n = 2312) were detected by mammography alone, 54.8% (n = 3470) by mammography and CBE, and 8.7% (n = 551) by physician-performed CBE alone (or 5.3% if considering ultrasonography). Invasive tumours diagnosed by CBE alone were more often triple-negative, HER2-positive, node-positive, and larger than those diagnosed by mammography alone ($p < 0.05$).

Conclusions A significant number of cancers would have been missed if CBE had not been performed. Compared with cancers detected by mammography alone, those detected by CBE had more aggressive features. Clinical breast examination is a very low-cost test that could improve the detection of breast cancer and could prompt breast ultrasonography in the case of a negative mammogram.

Key Words Breast cancer, clinical examination, mammography, ultrasonography, screening, palpable breast masses

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INTRODUCTION

Breast cancer is the most common cancer in women, with a lifetime probability of 11.5% and 24,400 new cases diagnosed in 2014 in Canada; however, by 2014, the mortality rate had decreased to 18.4 women per 100,000 from 30.7 women per 100,000 in 1984[1]. That decrease is in part a result of improvement in treatments and the implementation of screening programs. Indeed, compared with control subjects, women invited to screening had a 20% relative risk reduction for breast cancer mortality[2–4].

If screening mammography has been shown to lower breast cancer–specific mortality, controversy still remains with respect to clinical breast examination (CBE) in a screening context. Indeed, the Canadian National Breast Screening Study (CNBSS) concluded that there was no difference in 13- and 25-year survival between women who underwent screening using mammography plus CBE compared with CBE alone[5–7]; however, those conclusions should be considered in the light that a CBE was performed before randomization and that the CBE had to be normal[8]. Data derived from the Ontario screening program suggested that mammography and nurse-performed CBE result in a higher sensitivity than mammography alone, but with more false positives[9]; however, those results have minimal carryover in real-world practice because the CBEs in that study were performed by nurses who had received special training, a situation that would be clinically applicable only at the cost of great effort[10]. In general, 35% sensitivity for CBE is probably the best that can be achieved in community-based settings in the United States[11].

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The efficacy of CBE in reducing breast cancer mortality has not been shown by well-designed clinical trials[12]. Subsequently, many organizational guidelines (those from the Canadian Task Force on Preventive Health Care[13], the U.S. Preventive Services Task Force[12,14], the American Cancer Society[15], the U.K. National Health Services[16], and the World Health Organization[17]) removed CBE from their recommendations, although some still include it (specifically, those from the U.S. National Comprehensive Cancer Network[18], the American College of Obstetricians and Gynecologists[19], and Memorial Sloan Kettering Cancer Center[20]). In addition, in the presence of a normal mammogram and a palpable mass, many guidelines have been recommending targeted breast ultrasonography (BUS) of the palpable mass found at CBE[18,21,22]. Nevertheless, as in mammography screening, CBE offers professionals an opportunity to educate women about their breasts, the importance of early detection, the risks of breast cancer, and breast awareness.

It is a well-known fact that not all breast cancers are detected by screening mammography. In addition, screening mammography is not recommended for women of all ages[13,14,16–20]. To better understand the pertinence of CBE in routine clinical practice for breast cancer detection, the aim of the present study was therefore to determine the proportion of breast cancers diagnosed with CBE alone.

METHODS

Study Population

This retrospective study considered all women who were seen at the Centre des maladies du sein Deschênes-Fabia between July 1999 and December 2010, and who received a final diagnosis of breast cancer. Lobular carcinoma *in situ* and lobular neoplasia are not considered cancers[23] and were therefore not included in the analysis.

Data Collection

The Centre des maladies du sein Deschênes-Fabia maintains a registry of all breast cancer cases diagnosed at the centre since 1965. All histologically confirmed primary breast cancers treated at our centre are prospectively entered into the database by trained clerks. All patients undergo at least bilateral mammography and CBE as part of the routine staging procedure. In the presence of an abnormal CBE finding, BUS is performed; however, BUS results were added to the database only in 2006, even if the test had previously been performed.

All patients were categorized according to the presence of abnormalities observed at CBE or at mammography. A CBE was considered abnormal in the presence of a palpable mass, nipple discharge, skin or nipple retraction, edema, erythema, peau d'orange, or skin ulcers. In cases of multiple CBEs yielding different results in the context of the same work-up that led to the cancer diagnosis, only the worst results (that is, positivity for any of the enumerated symptoms or signs) are recorded in the database. An abnormal mammogram or BUS result was based on the interpretation of the radiologist and defined as either indeterminate or highly suggestive of malignancy. Tumour size was based on the pathology report.

At our centre during the study period, all CBEs were performed by surgeons ($n = 5$, 5–30 years of experience) and by general practitioners specialized in breast diseases ($n = 8$, 11–30 years of experience). However, the mammography or BUS might have been performed at our tertiary breast centre, at private radiology clinics, or at community hospitals.

Patients with an incomplete dataset were excluded ($n = 1342$). Included patients ($n = 6333$) were similar to the patients in the database overall ($n = 7675$) in terms of age (59.1 ± 12.3 years vs. 59.1 ± 12.2 years) and cancer type distribution [ductal carcinoma *in situ* (DCIS): 15.3% vs. 15.3%; invasive ductal carcinoma (IDC): 75.7% vs. 72.6%; invasive lobular carcinoma (ILC): 9.0% vs. 9.0%]. Patients in the BUS subset ($n = 3005$) were also similar to the patients in the database overall in terms of age (60.0 ± 12.5 years vs. 59.1 ± 12.3 years) and cancer type distribution (DCIS: 14.1% vs. 15.3%; IDC: 72.6% vs. 73.7%; ILC: 9.0% vs. 9.0%).

Statistical Methods

Descriptive statistics are used. Frequencies were compared using the Fisher exact test. Continuous variables were compared using analysis of variance with a Bonferroni *post hoc* test. The SAS software application (version 9.3: SAS Institute, Cary, NC, U.S.A.) was used to perform the analyses. Values of $p < 0.05$ were considered significant.

RESULTS

From July 1999 to April 2010, 7675 patients with new primary breast cancers were treated at our institution, but 1342 patients were excluded from the study because of an incomplete dataset. Among the 6333 remaining patients, 968 had DCIS (15.3%), 4795 had IDC (75.7%), 570 had ILC (9.0%), and 123 had other cancer types (2.2%).

All physical and imaging examinations were performed during the same time period and for the same reasons. Median time between CBE and mammography was 22.5 days (range: 0.0–357 days; interquartile range: 12–42 days). Median time between CBE and BUS was 12 days (range: 0.0–372 days; interquartile range: 3–33 days). Median time between mammography and BUS was 15 days (range: 0.0–339 days; interquartile range: 3–33 days). Thus, except for some outliers, all examinations were performed within a short time span.

In all patients considered here, cancer was detected (Figure 1) by mammography alone in 36.5% ($n = 2312$), by mammography and CBE in 54.8% ($n = 3470$), and by physician-performed CBE alone in 8.7% ($n = 551$).

In the patient subset with available BUS data that had been systematically entered into the registry (March 2006 to December 2010), cancer was detected by mammography alone in 17.4% ($n = 523$); by mammography and CBE in 12.7% ($n = 383$); by CBE and BUS in 9.8% ($n = 293$); by mammography and BUS in 16.1% ($n = 483$); by CBE, mammography, and BUS in 38.8% ($n = 1166$); and by CBE alone in 5.2% ($n = 157$). For invasive cancers only, pathologic tumour size of cancers diagnosed with CBE alone was 29.2 ± 27.1 mm compared with 26.2 ± 24.4 mm for cancers diagnosed by CBE and BUS ($p = 0.28$). Among the cancers detected by CBE but not by mammography nor by BUS, 79.0% were IDC, 14.0% were ILC, and 7.0% were other types.

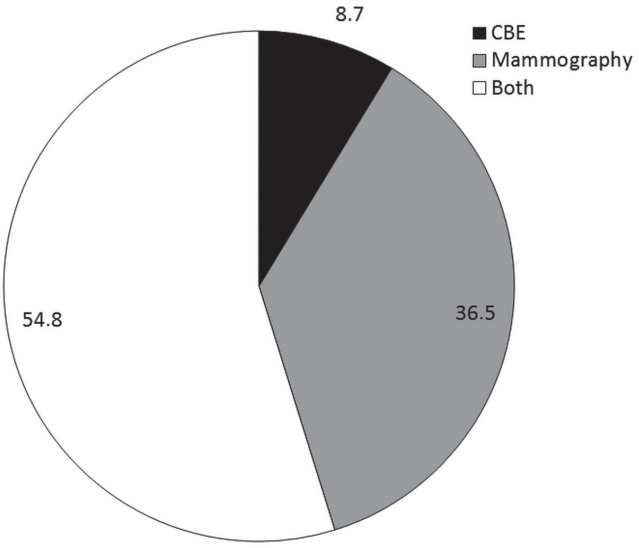

FIGURE 1 Proportion of cancers detected using clinical breast examination (CBE), mammography, or both (n = 6333).

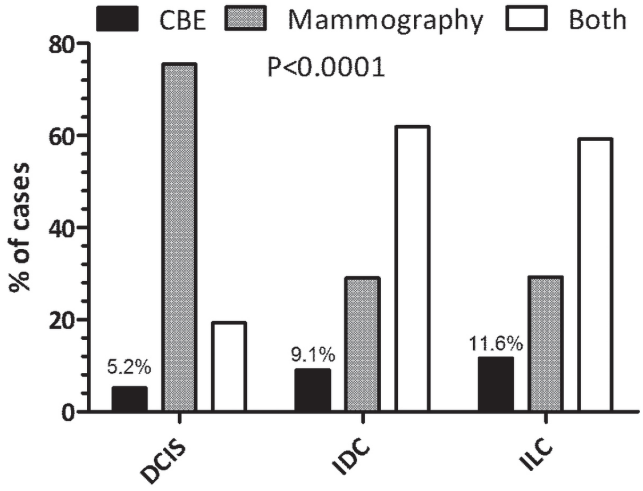

FIGURE 2 Proportion of cancers detected using clinical breast examination (CBE), mammography, or both, by histologic diagnosis. Compared with ductal carcinoma *in situ* (DCIS), invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) were more often diagnosed by CBE alone (difference between histologic diagnoses assessed by the Fisher exact test).

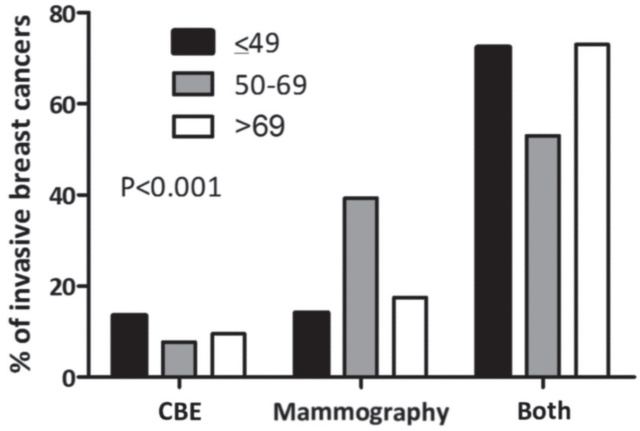

FIGURE 3 Proportion of cancers detected using clinical breast examination (CBE), mammography, or both, by age group. The proportion of invasive cancers detected using CBE alone was higher for patients 49 years of age and younger and for patients more than 69 years of age than for patients 50–69 years of age (differences between age groups assessed by the Fisher exact test).

Mode of detection differed by histologic diagnosis (Figure 2). Of the DCIS cases, 5.2% were detected using CBE alone, 75.5% using mammography alone, and 19.3% using both techniques. Of the IDC cases, 9.1% were detected using CBE alone, 29.0% using mammography alone, and 61.9% using both techniques. Of the ILC cases, 11.6% were detected using CBE alone, 29.2% using mammography alone, and 59.2% using both techniques.

The proportion of invasive cancers detected using CBE alone was higher for patients 49 years of age and younger (13.5%) and for patients more than 69 years of age (9.5%) than for patients 50–69 years of age (7.7%). Invasive cancers were more often detected using mammography alone in the 50–69 age group (39.3%) than in the younger and older patients (14.1% for those <50 years and 17.5% for those >69 years). Finally, use of both modalities detected a greater proportion of invasive cancers in patients 49 years of age and younger (72.4%) and in those more than 69 years of age (73.0%) than in those 50–69 years of age (53.0%; Fisher exact test: $p < 0.001$; Figure 3).

Node-negative cancers were more often detected using mammography alone (39.3% node-negative vs. 14.7% node-positive); node-positive cancers were more often detected using both modalities (52.7% node-negative vs. 75.5% node-positive); and slightly more node-positive cancers were detected using CBE alone (8.0% node-negative vs. 9.8% node-positive; Fisher exact test: $p < 0.001$; Figure 4).

Estrogen receptor–negative cancers (Fisher exact test: $p < 0.001$), progesterone receptor–negative cancers (Fisher exact test: $p < 0.001$), and HER2-positive cancers (Fisher exact test: $p = 0.002$) were more often detected using CBE alone or in combination with mammography or BUS (or both) than using mammography alone. In addition, more triple-negative cancers were detected using CBE alone or in combination with mammography or BUS, or both (Fisher exact test: $p < 0.001$; Figure 5).

Larger tumours were more often detected by CBE alone or in combination with mammography or BUS (or both); smaller tumours were more frequently detected using mammography alone (Fisher exact test: $p < 0.001$; Figure 6). In IDC and ILC cases, tumours detected using mammography alone were smaller than those detected using CBE alone or combined with mammography (IDC: 12.9 ± 9.2 mm for mammography alone vs. 23.5 ± 18.1 mm using CBE alone or 24.6 ± 15.3 mm for both; analysis of variance: $p < 0.05$; ILC: 16.2 ± 12.4 mm for mammography alone vs. 36.8 ± 39.8 mm for CBE alone or 32.3 ± 21.8 mm for both; analysis of variance: $p < 0.05$).

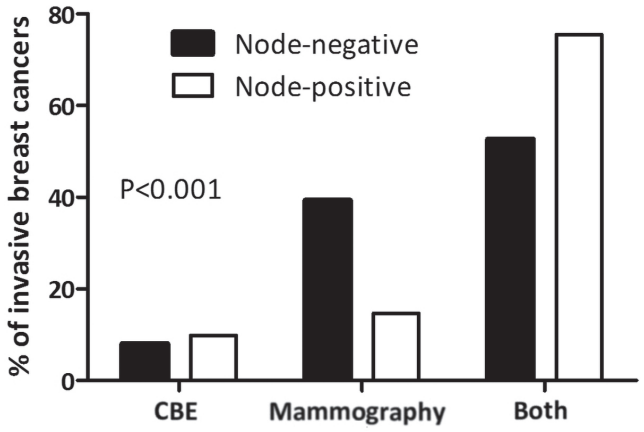

FIGURE 4 Proportion of cancers detected using clinical breast examination (CBE), mammography, or both, by lymph node status. More node-negative cancers were detected using mammography alone; more node-positive cancers were detected using both modalities; and slightly more node-positive cancers were detected using CBE alone (differences in lymph node status assessed by the Fisher exact test).

DISCUSSION

Of all patients considered in the present analysis, 36.5% were detected by mammography alone, 54.8% by mammography and CBE, and importantly, 8.7% by physician-performed CBE alone. Even considering the subset of cancers with available BUS data, 5.2% of cancers were still detected by CBE alone. In addition, if DCIS is excluded, the importance of CBE becomes even more pertinent (9.1% for IDC and 11.6% for ILC vs. 5.2% for DCIS). Finally, cancers with aggressive features were more often detected using CBE than using mammography alone.

No previous study has assessed the effect of the learning curve on physician efficiency in discovering breast abnormalities, but it is a reasonable assumption that physicians regularly performing CBE will be better at it. Trainees who underwent comprehensive training were more proficient at finding abnormalities in silicone breast models[24] and were more comfortable when performing the examination[25]. In addition, to be called "new," a lesion must be compared with a previous examination. A physician who does not practice CBE regularly will therefore be unable to reassure the patient.

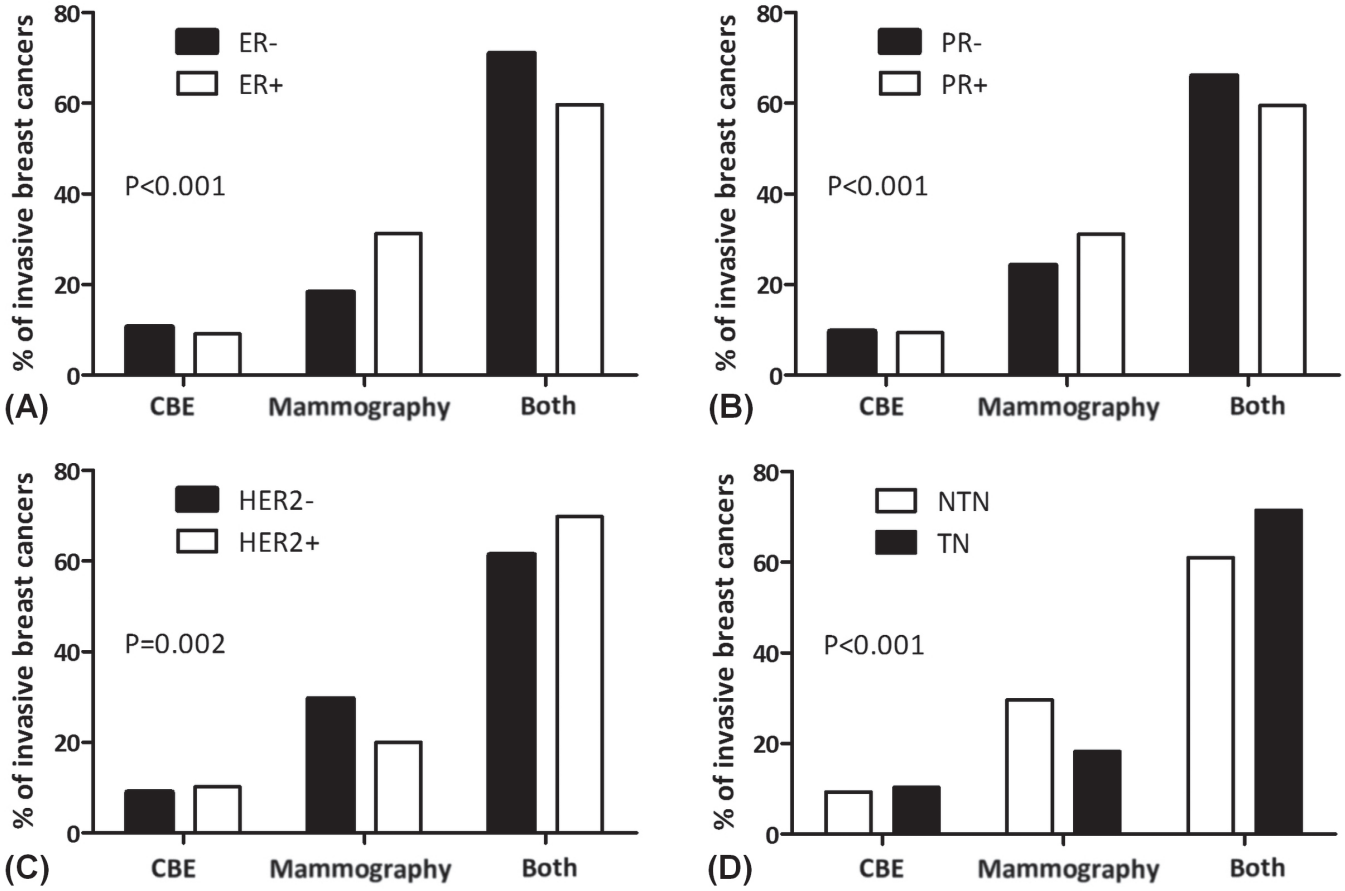

FIGURE 5 Proportion of cancers detected using clinical breast examination (CBE), mammography, or both, by hormone receptor status. Compared with mammography alone, CBE (alone or in combination with mammography) detected (A) more estrogen receptor (ER)–negative cancers, (B) more progesterone receptor (PR)–negative cancers, (C) more HER2-positive cancers, and (D) more triple-negative (TN) cancers (differences between negativity and positivity assessed by the Fisher exact test). NTN = non-TN.

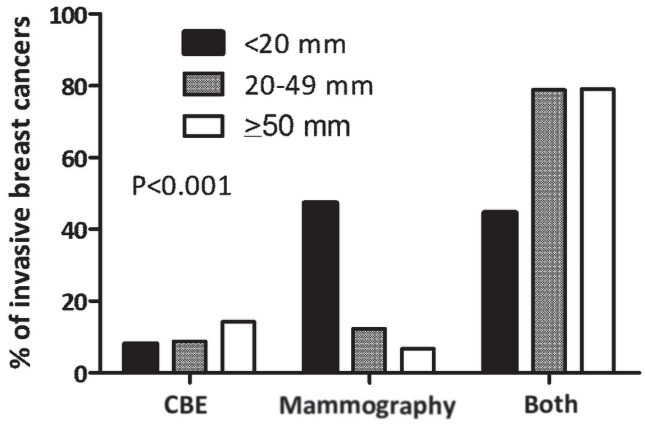

FIGURE 6 Proportion of cancers detected using clinical breast examination (CBE), mammography, or both, by tumour size. Larger tumours were more often detected by CBE (alone or in combination); smaller tumours were more frequently detected by mammography alone (differences between tumour size groups assessed by the Fisher exact test).

In the detection of breast cancer, CBE, with sensitivity of 54% and specificity of 94%, contributes independently from mammography[11]. A study showed that the sensitivity of CBE in clinical practice was 28%–36% compared with the sensitivity of 63% observed in the CNBSS[26]. That huge difference could be a result of training, given that the CNBSS nurses and physicians were highly trained for the study. It also supports the suggestions that physicians should be properly trained for CBE and that suspicious cases should be referred to a dedicated breast disease centre. In the present study, all CBEs were performed by highly experienced physicians.

In the 1960s, the HIP study showed that the combination of mammography and CBE by trained surgeons led to a reduction in breast cancer mortality[27]. In that study, cancer detection by mammography in young women was low, and advanced disease was more often detected by CBE[28]. However, one of the most important studies evaluating breast cancer screening, the CNBSS, did not include a group for evaluating the efficacy of CBE alone[29]. The CNBSS compared the combination of mammography, CBE, and breast self-examination (BSE) with combined CBE and BSE. No significant benefit in young women (40–49 years) was observed[7]. Mammography with CBE and BSE detected cancers at an earlier stage than did CBE with BSE, but no mortality benefit in women 50–59 years of age was observed[6]. A study by Rijnsburger *et al.*[30] showed that CBE with BSE should lower breast cancer mortality by 20% in women 50–59 years of age, but no adjustment was made for hormonal therapy and chemotherapy. In the province of Quebec, breast cancer screening with mammography has been offered to women 50–69 years of age since 1998, and that initiative could explain why our study shows that mammograms were more frequently positive in that age group.

In 1998, Elmore *et al.*[31] showed that the false-positive rate after 10 screening mammograms was 49.1%; it was 22.3% after 10 screening CBEs. Furthermore, Bancej *et al.*[32] demonstrated that CBE was the reason for 28.5%–36.7% of all referrals, and mammography, for 52.6%–60.1%; but CBE resulted in 4.6%–5.9% of detected cancers, and mammography, in 60.0%–64.3%. Referrals resulting from CBE therefore led to a higher burden to the health system, but also led to more breast cancers being detected. The increased detection of 3–10 small cancers per 100,000 screens might seem to some authors to be a minimal contribution[32], but we consider that each cancer detected at an early stage, particularly aggressive HER2-positive cancers for which anti-HER2 therapies are now available, might offer better outcomes to some patients. A Japanese study suggested that screening CBE should be added to mammography, but that it might be omitted in women 60–70 years of age[33], with the best trade-off between the sensitivity and specificity of CBE being observed in women 40–50 years of age. A careful socioeconomic analysis of the burden to the health system from over-referral compared with the savings from detecting and treating breast cancers earlier should be performed; all women should be analyzed, including those too old to be targeted by screening programs.

Nevertheless, when considering mammography and CBE, 8.7% of breast cancers in the present study would have been missed if CBE had not been performed—a finding that is supported by previous studies[9,32,34]. In the present study, a positive CBE was most often associated with estrogen receptor–negative, progesterone receptor–negative, HER2-positive breast cancers and with triple-negative breast cancers, which is supported by previous studies[34,35]; however, the relation with HER2 positivity is controversial[34]. In addition, another study showed that 13% of women with a palpable breast mass and a diagnosis of invasive cancer had had a normal mammogram within the preceding year[36]. Interval cancers often show aggressive features[37], and it is not impossible that some of the cancers detected by CBE alone in the present study were interval cancers. Triple-negative cancers are often found in *BRCA* mutation carriers, but according to a systematic review[38], the exact value of CBE for hereditary cancers might be controversial. Finally, a body of evidence is currently emerging for the role of screening CBE in women at high risk for breast cancer—for example, *BRCA* carriers and women with a lifetime risk of breast cancer exceeding 25%[39]. Those issues warrant further studies.

Preliminary data showed that, in developing countries in which CBE is often the only available screening modality, a shift in cancer staging at diagnosis is being achieved in women not targeted by any screening program[40]. The present study, supported by results from previous reports, therefore strongly suggests and emphasizes the importance of performing CBE, because it is the only technique detecting breast cancer in some patients, mainly women who are not targeted by screening programs. In addition, a learning curve is associated with CBE, and physicians should regularly perform CBE to maintain high detection standards.

An important issue to be emphasized is that, when a symptom is present, CBE must be performed before any additional imaging or other examinations are sought. Indeed, a previous study showed that about 11% of women

complaining of the presence of a breast mass had a cancer, as did about 4% of women with any complaints about their breasts[41]. However, a physician who does not perform CBE regularly will have more difficulty in executing the technique correctly and will need more examinations and imaging, increasing costs and perhaps postponing a diagnosis by not ordering tests for those women. Although the present study was not designed to determine if CBE could be added as a screening tool for the general population, our results suggest that CBE should be performed for women with symptoms and should be part of the opportunistic screening in women without symptoms but taking hormone replacement therapy; in women at higher risk, such as young women with dense breasts, familial history, mutation, history of atypical breast lesion, and history of breast cancer[42]; and possibly also in older women who are less likely to undergo mammographic screening compared with younger women, given that a strong association between older age and delayed diagnosis has been observed[43]. Nevertheless, screening CBE could be proposed to women who refuse to participate in mammographic breast cancer screening programs. We must raise the issue that physicians in training are no longer systematically trained in performing CBE despite the availability of new training technologies that emulate diseased breasts[42]. In light of the present study and based on recent recommendations against CBE[12–14,16,17], some breast cancers will probably be found at late stages in the future.

Because of the controversy about whether to perform CBE, no guideline recommends an optimal and validated CBE method. Data support the performance of CBE using the vertical strip method instead of the circular ("clock") pattern[44,45]. In addition, the use of 3 fingers, of 3 distinct pressure levels, of a visual examination of the breast, and of an axillary examination should be encouraged[46]. Nevertheless, some authors argue that, despite all efforts at improvement, CBE will still be limited with respect to the minimal lesion size detectable[47]; however, the Munich Field Study showed that, compared with no early detection, CBE and BSE seemed to favourably affect the stage of cancers being detected[48].

The present study is not without limitations. Indeed, it was a retrospective study in a tertiary breast cancer centre limited to the variables available in our database. Data came from a single centre, introducing the possibility of biases in the performance of the CBE itself or in documenting results. The CBEs were performed by various physicians and surgeons with different experience levels in CBE. The study was performed during a period of major changes in imaging techniques. Mammography evolved from analog techniques at the beginning of the study period to computed radiology techniques by the end of the period, which could have led to a higher number of cancers being detected by mammography in the late period of the study[49]; however, digital radiology systems were acquired just after the period covered by this present study. Similarly, the BUS examinations were performed using different units showing great variety in spatial and contrast resolution. In addition, the BUS examinations were performed by radiologists with a wide range of experience in various clinical settings. The BUS results were compiled into the database starting only in 2006, but the subset of cancers with BUS data available was comparable to the overall study sample. As recommended by many organizations and in many guidelines, a positive CBE should always prompt targeted BUS[21,22]. Breast density was not available in the database. Finally, our database records the results of only the physical examination that was part of the work-up that led to the diagnosis of cancer, without taking into account earlier examinations and without differentiating between a woman who presented because she herself found a mass or because the physician found a mass during a routine checkup. However, the results recorded in the database are those of the CBE performed by the physicians at our institution; in addition, because cancer patients are always first seen at least by a general practitioner on the team and then by a surgeon, the likelihood of eventually finding a mass, if it is present, might increase.

CONCLUSIONS

A significant number of the records for the breast cancer patients in our institution's database showed that the tumours were not detected using mammography and would have been missed if a CBE had not been performed. Performed by a trained physician, CBE is important for detecting breast cancers. Clinical breast examination is a very low-cost test that could improve the detection of breast cancer. For patients with breast symptoms, a CBE has to be performed. Furthermore, CBE should be a part of routine periodic examinations, especially for women less than 50 and more than 69 years of age, for moderate- and high-risk women, and for women who have had a breast cancer. When a CBE is positive, BUS is mandatory, regardless of the mammography result. We are worried that many guidelines and task forces are removing CBE from their recommendations about routine examinations without distinction for high-risk patients, as already discussed. Physicians should be proficient in CBE, and practice is needed to be proficient. It would be bad if some cancers were detected at late or inoperable stages only because a CBE was not performed.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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