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資料編・用語編

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資料編
・乳がん患者コホート研究
国立がん研究センターでのパイロット研究
・L1/L2付録実証性研究

用語編
・コホート研究

国立がん研究センターの乳がん患者さんでのパイロット研究

1. パイロット(試験的)研究について

わたしたちは、乳がん患者コホート研究に先駆けて、お尋ねする質問が適切なものか、患者さんが質問票に回答することをどのように感じているかなどを調べるための試験的な研究(パイロット研究)を2006年に行いました。

ご協力いただいたのは、国立がん研究センター乳癌外科・内科で診療中の乳がん患者さん125人(入院44人、外来81人)です。このパイロット研究の結果、この研究の実施可能性が示されるとともに、食事や運動などの生活習慣や、代替療法の利用について、興味深い結果が得られました。以下に結果の概要をご紹介します。

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2. 生活習慣の変化

乳がんになって以降、多くの患者さんで、大豆食品や緑黄色野菜、果物を多くとるようになり、肉製品やお酒、たばこを減らすようになったという回答が得られ、患者さんの食生活に関する関心の強さや、再発を防ぐためにご自身の生活を変えようとする思いがうかがわれました。

下の図は、外来の患者さん81人の回答です。

生活習慣の変化(外来患者81名)

食品・習慣	増加/減少の割合 (%)
肉製品	減少 (約 15%)
大豆食品	増加 (約 15%)
緑黄色野菜	増加 (約 15%)
果物	増加 (約 15%)
お酒	減少 (約 15%)
たばこ	減少 (約 15%)

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コホート研究とケース・コントロール研究

コホート研究は、ケース・コントロール研究と並ぶ疫学の代表的な研究方法です。

疫学とは、人間集団を対象に健康に関わる要因を明らかにする学問です。たとえば、初経年齢が早い人、出産経験のない人、初産年齢の遅い人、閉経年齢の遅い人などは乳がんになりやすいと言われていますが、このような要因は疫学研究によって明らかになったものです。以下、乳がんを例にこれらの手法を紹介します。

ケース・コントロール研究は、乳がん患者さんをケース群、年齢などの条件を同じに揃えたがんをたない人をコントロール群として、初経年齢など乳がんとの関連が疑われる要因について調査し、2群の間で比較するものです。この方法は調査期間が比較的短く、結果が早くわかるという利点がありますが、一方で適切なコントロール群の設定が難しいこと、過去に遡って要因を調べることに伴いさまざまな偏りが入り込む可能性が高いこと、などが問題となります。

コホート研究は、はじめにがんをたない健康な人々の集団に対して、初経年齢など乳がんとの関連が疑われる要因について調査し、初経年齢の早い人々と遅い人々との間で、その後乳がんになった人の人数を比較するものです。これは、一般に大規模な集団を長期にわたって調査する必要がありますが、要因についての調査をした後にがんの発症を把握するという方法であるため、ケース・コントロール研究よりも偏りが入りにくい、比較的信頼性の高い方法とされています。

またコホート研究では、がんの発症に関連する要因の研究だけでなく、調査集団をがん患者さんに、乳がんの発症をがんの再発やQOL(クオリティオブライフ、生活の質)に置き換えることで、どのような人が再発しにくいのか、またQOLが高いのかといったことも検討できます。

このように、研究方法によって一長一短はありますが、疫学研究からのエビデンスが蓄積することによって、乳がんの発症や再発を予防したり、乳がん患者さんのQOLを高めたりするためにどうすればよいか、ということが明らかになります。

付録 8

研究紹介リーフレット



希望の虹プロジェクト

全国の乳がん患者さん**1万人**を目標に ご協力をお願いしています

患者さんひとりひとり、がんの治療方法が異なるように、
術後の生活や経過、再発の有無も、人それぞれです。
ひとりひとり、みな違うからこそ、
確実な結果を得るために、1人でも多くの方のご協力が必要です。

ご協力をお願いしたいこと

年に1度「生活習慣や代替療法に関する質問票」に回答ください。
ご協力いただくのは1回から、最も多いかたで5回となります。

質問票は、ご回答頂く時期が来たら主治医から直接お渡しします。

また、主治医の協力のもと、あなたの治療情報とその後の経過に
ついての情報を収集することをご了承ください。

調査に参加することによる、参加者 個人への直接の利益はありません

本調査の主な目的は、結果を将来の乳がんのよりよい予防・治療法の確立につなげて
いくことです。但し、ご回答頂いた日々の食生活については、

ひとりひとり栄養計算をした上で、結果をお返しさせていただきます。

(写真)

Q&A

Q 調査に参加することで、普段の生活でしなければならないこと、
気をつけないといけないことはありますか？

A 質問票へのご回答以外に、調査のために何かを行っていただく必要はありません。
普段どおりに生活してください。

Q その時々で生活習慣や気持ちが変わることもあるのですが、
調査に参加しても問題ないですか？

A 問題ありません。食生活や運動習慣などは、1年間のだいたいの平均的な生活について、
お気持ちなどについては、その時々の状態・状況をお答え下さい。

Q 調査の結果は、いつごろ明らかになりますか？

A 2020年に結果を出すことを目指して進めています。研究結果は、学術雑誌や学会、
ホームページにて公表し、乳がん患者さんの支援や医学の発展に役立てていく予定です。

この研究は、厚生労働省などから研究助成を受けて実施されています
(平成19年度、平成22年度厚生労働科学研究費補助金がん臨床研究事業(研究代表者:山本精一郎))。
この研究に関するより詳しい説明や、この研究の途中経過、研究結果をご覧になりたい方は、
CSPORホームページ(<http://www.csp.or.jp/network/cohort>)をご参照いただくか、下記までご連絡ください。
また、ご不明な点や疑問、不安があるときなども、コールセンターにいつでもお気軽にご連絡ください。

コールセンター コホート06担当 NPO法人日本臨床研究支援ユニット (J-CRSU) 内

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受付時間: 平日10時~17時(祝祭日、年末年始を除く)

住所: 〒113-0034 東京都文京区湯島1-9-5 御茶ノ水小柳出ビル

乳がん再発を防止するために 生活習慣や代替療法に関する調査 ご協力のお願い

あなたの主治医と国立がん研究センターが
共同で進めている調査です

(研究責任者)
国立がん研究センター
山本精一郎

生活習慣を変えると 乳がんの再発を防げる

可能性があると言われてます。
では、乳がんの再発を防ぐために…

“どんな食品を避けたほうが
いいの？”

“サプリメント等の代替療法は本当に
再発防止に効果があるの？”

“ストレスと再発は関係するの？”

あなたの経験が、 これからの乳がん患者さんの “ちから”になる。

皆さんの生活習慣や代替療法、その時々のお気持ちの状態などと
治療の経過との関係を調べさせていただくことで、
再発を予防するために効果的な生活を科学的に明らかにしま

どの食品は避けるべきか。

数ある代替療法それぞれの効果の有無。

どのような心理状態で生活するのが
望ましいのか。

それは、医学の発展に役立つとともに
これからの乳がん患者さんの、大きな指針となるはずです。

皆さんが同じ悩みを抱えています。しかし、
ところ、どのような生活が再発予防に効果的
学的根拠は十分には得られていません。

III. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

【雑誌】

発表者名	論文タイトル名	発表誌名	巻号	ページ	出版年
<u>Mizota Y, Yamamoto S.</u>	Prevalence of Breast Cancer Risk Factors in Japan.	Jpn J Clin Oncol	42(11)	1008-12	2012
Shimizu C, Bando H, Kato T, <u>Mizota Y, Yamamoto S,</u> Fujiwara Y.	Physicians' knowledge, attitude, and behavior regarding fertility issues for young breast cancer patients: a national survey for breast care specialists.	Breast Cancer	20(3)	230-40	2013
Nozawa K, Shimizu C, Kakimoto M, <u>Mizota Y, Yamamoto S,</u> Takahashi Y, Ito A, Izumi H, Fujiwara Y.	Quantitative assessment of appearance changes and related distress in cancer patients.	Psychooncology	in press		2013
Itoh H, <u>Iwasaki M,</u> Sawada N, Takachi R, Kasuga Y, Yokoyama S, Onuma H, Nishimura H, Kusama R, Yokoyama K, Tsugane S.	Dietary cadmium intake and breast cancer risk in Japanese women: A case-control study.	International journal of hygiene and environmental health	in press		2013
<u>Sawaki M,</u> Mukai H, Tokudome N, Nakayama T, Taira N, Mizuno T, Yamamoto Y, Horio A, Watanabe T, Uemura Y, <u>Ohashi Y.</u>	Safety of Adjuvant Trastuzumab for HER2-overexpressing Elderly Breast Cancer Patients: A multicenter cohort study.	Breast Cancer	19	253-8	2012
溝田友里, 山本精一郎	がん患者コホート研究：予後改善へのエビデンス	医学のあゆみ	241(5)	384-90	2012
溝田友里, 山本精一郎	日本における乳がんの疫学的動向	日本臨牀	70(増刊号7)	37-41	2012
溝田友里, 山本精一郎	がん予防のためのソーシャルマーケティング手法	体育の科学	62(2)	109-18	2012
Ohuchi N, Ishida T, Kawai M, Narikawa Y, <u>Yamamoto S,</u> Sobue T.	Randomized controlled trial on effectiveness of ultrasonography screening for breast cancer in women aged 40-49 (J-START): research design.	Jpn J Clin Oncol	41(2)	275-7	2011
Fujii H, <u>Yamamoto S,</u> Takeda-Imai F, Inoue M, Tsugane T, Kadowaki T, Noda M.	Validity and applicability of a simple questionnaire for the estimation of total and domain-specific physical activity.	Diabetology International	2	47-54	2011

発表者名	論文タイトル名	発表誌名	巻号	ページ	出版年
Tanai C, Eguchi Nakajima T, Nagashima K, Kato K, Hamaguchi T, Yamada Y, Muro K, Shirao K, Kunitoh H, Matsumura Y, <u>Yamamoto S</u> , Shimada Y.	Characteristics and Outcomes of Patients With Advanced Gastric Cancer Who Declined to Participate in a Randomized Clinical Chemotherapy Trial.	J Oncol Practice	7(3)	148-53	2011
<u>Iwasaki M</u> , Tsugane S.	Risk factors for breast cancer: epidemiological evidence from Japanese studies.	Cancer Sci	102	1607-14	2011
Suzuki R, <u>Iwasaki M</u> , <u>Yamamoto S</u> , et al.	Leisure-time physical activity and breast cancer risk defined by estrogen and progesterone receptor status-The Japan Public Health Center-based Prospective Study.	Prev Med	52	227-33	2011
<u>Iwasaki M</u> , Kasuga Y, Yokoyama S, et al.	Comparison of postmenopausal endogenous sex hormones among Japanese, Japanese Brazilians, and non-Japanese Brazilians.	BMC Med	9	16	2011
<u>Sawaki M</u> , Tokudome N, Mizuno T, Nakayama T, Taira N, Bando H, Murakami S, Yamamoto Y, Kashiwaba M, Iwata H, Uemura Y, Ohashi Y.	Evaluation of Trastuzumab Without Chemotherapy as a Postoperative Adjuvant Therapy in HER2 Positive Elderly Breast Cancer Patients: N-SAS BC 07 (RESPECT study).	Jpn J Clin Oncol	41	709-12	2011
溝田友里, <u>山本精一郎</u>	ソーシャルマーケティングを活用したがん予防行動の「普及」の試み.	公衆衛生情報	40(12)	26-9	2011
<u>Iwasaki M</u> , Hamada GS, Nishimoto IN, Netto MM, Motola J Jr, Laginha FM, Kasuga Y, Yokoyama S, Onuma H, Nishimura H, Kusama R, Kobayashi M, Ishihara J, <u>Yamamoto S</u> , Hanaoka T, Tsugane S.	Dietary isoflavone intake, polymorphisms in the CYP17, CYP19, 17 β -HSD1 and SHBG genes, and risk of breast cancer in case-control studies in Japanese, Japanese Brazilians, and non-Japanese Brazilians.	Nutr Cancer	62	466-75	2010
Toi M, <u>Ohashi Y</u> , Sweow A, Moriya T, Tse G, Sasano H, Park BW, Chow LWC, Laudico AV, Yip CH, Ueno E, Ishiguro H, Bando H.	The Breast Cancer Working Group Presentation was Divided into Three Sections: The Epidemiology, Pathology and Treatment of Breast Cancer.	Jpn J Clin Oncol	40 (Supplement 1)	i13-i18	2010
<u>Iwasaki M</u> , Inoue M, Sasazuki S, Sawada N, Yamaji T, Shimazu T, Willett WC, Tsugane S.	Green tea drinking and subsequent risk of breast cancer in a population to based cohort of Japanese women.	Breast Cancer Res	12	R88	2010

発表者名	論文タイトル名	発表誌名	巻号	ページ	出版年
山本精一郎	がん臨床試験の生物統計学	産科と婦人科	77(5)	495-502	2010
溝田友里, 山本精一郎	乳がん疫学の最新の動向	最新医学	65(6月増刊号)	1251-63	2010
山本精一郎	研究倫理と被験者保護：国内外における現状と今後の方向性.	血液・腫瘍科	60(5)	667-72	2010

【書籍】

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
山本精一郎, 平成人, 岩崎基 (作成委員)		日本乳癌学会	患者さんのための乳がん診療ガイドライン 2012年版.	金原出版	東京	2012	
山本精一郎, 溝田友里	わが国の乳癌リスクファクターの推移.	園尾博司 (監修)	これからの乳癌診療 2012~2013	金原出版	東京	2012	111-7
山本精一郎, 岩崎基 (作成委員)		日本乳癌学会	科学的根拠に基づく乳癌診療ガイドライン② 疫学・診断編 2011年版.	金原出版	東京	2011	

IV. 研究成果の刊行物・別刷

Original Article

Prevalence of Breast Cancer Risk Factors in Japan

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Objective: Breast cancer is the most common type of cancer in women worldwide. Although the incidence of breast cancer is still on an increasing trend, there are few studies concerning breast cancer risk factors in Japan. Therefore, we conducted an Internet survey investigating the prevalence of risk factors for breast cancer.

Methods: We conducted an Internet survey using opt-in panels in women aged from 20 to 70 years. The survey items consisted of potential and proven risk factors for breast cancer such as age at menarche, menopausal status, premenopausal use of oral contraceptives, postmenopausal use of hormones, parity, height, alcohol consumption and family history of breast cancer.

Results: Subjects comprised 2002 persons who were matched for sex, age and residential area with the National Census in 2005. Statistically significant trends were observed for most factors: age at menarche is becoming lower, age at first birth is higher, height is higher, the proportion of women who have given birth is smaller and the proportion of women who drink alcohol is larger.

Conclusions: We showed a clear increase in the prevalence of risk factors for breast cancer. Based on the results, the incidence of breast cancer in Japan may be increasing for at least a few decades.

Key words: breast cancer – incidence – risk factors – Japan – Asia

INTRODUCTION

Breast cancer is the most common type of cancer in women worldwide. According to the International Agency for Research on Cancer, an estimated 1 150 000 patients were newly diagnosed with breast cancer in 2002. Furthermore, breast cancer has the highest cancer-related mortality rate among women. In 2002, 410 000 women died of breast cancer (1). In Japan, 11 918 women died of breast cancer in 2009, leading to an age-adjusted mortality rate of 11.8 per 100 000 population. In 2006, the age-adjusted incidence rate of female breast cancer in Japan was estimated as 60.3 per 100 000 population, second highest to colorectal cancer. The age-adjusted incidence rate of breast cancer has markedly increased in Japan (2).

A number of risk factors for breast cancer have been identified, including hereditary predispositions such as a family history of breast cancer and *BRCA1/BRCA2* mutations, endocrine environmental factors regarding menarche and menopause, socio-environmental factors such as parity and lactation, and lifestyle-related factors such as obesity, physical activity level and alcohol consumption. The evidences for various lifestyle-related risk factors in breast cancer were reviewed by the World Cancer Research Fund and the American Institute for Cancer Research and those relevant for Japanese women by Japanese researchers (3,4).

Unfortunately, however, few studies have evaluated the prevalence of risk factors for breast cancer in Japanese

women and how they change over time. The JNHS is a large-scale epidemiological cohort study involving female Japanese nurses (5) which investigated risk factors for breast cancer, including menstruation, parity and the use of hormones. However, nurse-specific factors such as the use of hormones and night duty were frequent; the subjects are not entirely representative of the general population of Japanese women. Furthermore, the height and alcohol intake of Japanese women have been investigated every year by the Ministry of Health, Labour and Welfare through the National Health and Nutrition Survey (6). It involves ~6 000 households and household members in 300 areas throughout Japan in accordance with the Health Promotion Law, which mandates the collection of data regarding the national physical state, nutritional intake and lifestyle-related factors in order to comprehensively promote national health. However, no data on other risk factors for breast cancer have been collected in that survey.

Recently, the widespread use of the Internet has facilitated the sampling of subjects representative of the Japanese population with respect to geographical and age distributions. However, it is necessary to examine whether or not these subjects are truly representative of the Japanese population because they are limited to persons who can access the Internet. If there is no association between Internet usage and the prevalence of risk factors, Internet surveys can provide representative data.

Among potential and proven risk factors for breast cancer, risk factors such as age at menarche, age at menopause, age at first birth, number of children and height became unchanged once a woman has reached a specific age. Therefore, the prevalence of these factors at or above this age in a cross-sectional survey can be considered to represent cohort effects rather than age effects. Future trends in the incidence of breast cancer can be predicted to some extent by investigating the trends involving these risk factors. As for variables such as nutrient intake and body weight, which may change with age, their prevalence reflects both cohort and age effects. Therefore, it is difficult to use data from cross-sectional surveys for future prediction of breast cancer incidence, but it is still useful to calculate the risk of breast cancer at the time of a cross-sectional survey using prediction models such as the Gail model (7). Using these risk scores, the size of a population at high risk for breast cancer can be identified.

Therefore, in order to clarify the prevalence of risk factors for breast cancer in Japanese women, we conducted a study investigating the distribution of potential and proven risk factors using a cross-sectional Internet survey.

PATIENTS AND METHODS

DATA COLLECTION

We conducted an Internet survey in which the subjects were women between the ages of 20 and 70 who participated in

opt-in (registered by the subjects themselves) panels. It has been pointed out that Internet surveys have problems associated with duplicated answers and socioeconomic bias (8–11). In Japan, an age bias has been reported (12). However, the opt-in panels used in this study verify the survey logic, so duplicated answers can be avoided (13,14). Among the panels, 2002 people were recruited until sex, age and residential area distribution were the same as the National Census in 2005. The survey was conducted between 15 and 20 February 2008.

SURVEY ITEMS

The survey consisted of potential and proven risk factors for breast cancer such as age at menarche, menopause status, premenopausal use of oral contraceptives, postmenopausal use of hormones, parity, height, alcohol consumption and family history of breast cancer. Data of other potential risk factors such as dietary factors were also collected, but they were not reported here since their evidence concerning associations with breast cancer incidence are still limited (3,4).

STATISTICAL ANALYSIS

Trends of the prevalence of risk factors over birth year were examined using ANOVA for continuous variables and the Cochran–Mantel–Haenszel test for categorical variables. Two-sided value of $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SAS software 9.2 (SAS Institute, Cary, NC, USA).

RESULTS

The background characteristics of the subjects are shown in Table 1. The proportion of smoker and that of full-time worker were higher in younger age groups. Younger age groups had higher educational background.

The most frequent age at menarche was 12 years. Women who experienced menarche between the ages of 12–14 years accounted for ~70% of the sample (Table 2). The age at menarche was 11 years or younger in <20% of the subjects. With respect to age, the mean age at menarche was ~14 years in women who were born in or around 1938 (age at the time of the survey, 70 years). It was ~12 years in those who were born in or around 1988; the appearance of menarche was earlier in younger subjects (P value for trend <0.001).

Postmenopausal women accounted for 65% of the subjects aged 50–59 years (Table 2). In ~10% of those aged 50 years or older, menopause was surgically induced. There was no clear trend between age at menopause and birth year (P value for trend 0.18).

Of all responders, 70% had given birth (Table 2). In ~50% of women who have given birth, the age at first birth ranged from 25 to 29 years. It was 30 years or older in 17.1% of the respondents. Among subjects who were born

Table 1. Background characteristics of the subjects

	Total (n = 2002)	≤1938 (age ≥70) (n = 86)	1939–1948 (age 60–69) (n = 677)	1949–1958 (age 50–59) (n = 344)	1959–1968 (age 40–49) (n = 292)	1969–1978 (age 30–39) (n = 337)	1979–1988 (age 20–29) (n = 266)
Smoking (%)							
Smoker	309	2 (2.3)	69 (10.2)	67 (19.5)	59 (20.2)	63 (18.7)	49 (18.4)
Quitter	257	5 (5.8)	79 (11.7)	37 (10.8)	39 (13.4)	54 (16.0)	43 (16.2)
Nonsmoker	1436	79 (91.9)	529 (78.1)	240 (69.8)	194 (66.4)	220 (65.3)	174 (65.4)
Education (%)							
Junior high school	44	8 (9.3)	21 (3.1)	2 (0.6)	3 (1.0)	5 (1.5)	5 (1.9)
High school	669	21 (24.4)	190 (28.1)	138 (40.1)	120 (41.1)	134 (39.8)	66 (24.8)
Junior college	733	39 (45.4)	325 (48.0)	108 (31.4)	99 (33.9)	97 (28.8)	65 (24.4)
University	500	9 (10.5)	128 (18.9)	89 (25.9)	65 (22.3)	95 (28.2)	114 (42.9)
Graduate school	26	0 (0.0)	6 (0.9)	3 (0.9)	4 (1.4)	3 (0.9)	10 (3.8)
Other	30	9 (10.5)	7 (1.0)	4 (1.2)	1 (0.3)	3 (0.9)	6 (2.3)
Occupation (%)							
Full time	407	3 (3.5)	57 (8.4)	74 (21.5)	78 (26.7)	100 (29.7)	95 (35.7)
Part time	408	4 (4.7)	82 (12.1)	90 (26.2)	95 (32.5)	72 (21.4)	65 (24.4)
Housewife	833	53 (61.6)	381 (56.3)	136 (39.5)	86 (29.5)	133 (39.5)	44 (16.5)
Self-employed	108	5 (5.8)	44 (6.5)	25 (7.3)	19 (6.5)	13 (3.9)	2 (0.8)
Unemployed/ student	192	19 (22.1)	91 (13.4)	4 (1.2)	6 (2.1)	13 (3.9)	59 (22.2)
Other	54	2 (2.3)	22 (3.3)	15 (4.4)	8 (2.7)	6 (1.8)	1 (0.4)
Family income per year (%)							
<1 000 000 yen	49	5 (5.8)	23 (3.4)	3 (0.9)	2 (0.7)	4 (1.2)	12 (4.5)
<3 000 000 yen	332	28 (32.6)	120 (17.7)	40 (11.6)	36 (12.3)	50 (14.8)	58 (21.8)
<6 000 000 yen	767	38 (44.2)	261 (38.6)	104 (30.2)	96 (32.9)	171 (50.7)	97 (36.5)
<9 000 000 yen	442	9 (10.5)	134 (19.8)	84 (24.4)	96 (32.9)	72 (21.4)	47 (17.7)
<12 000 000 yen	260	4 (4.7)	83 (12.3)	71 (20.6)	42 (14.4)	30 (8.9)	30 (11.3)
≥12 000 000 yen	152	2 (2.3)	56 (8.3)	42 (12.2)	20 (6.9)	10 (3.0)	22 (8.3)

Age is calculated at the end of 2008.

Table 2. Prevalence of breast cancer risk factors by birth year in Japanese women

	Total			≤1938 (age ≥70)			1939–1948 (age 60–69)			1949–1958 (age 50–59)			1959–1968 (age 40–49)			1969–1978 (age 30–39)			1979–1988 (age 20–29)			Trend
	n	Mean	SE	n	Mean	SE	n	Mean	SE	n	Mean	SE	n	Mean	SE	n	Mean	SE	n	Mean	SE	
Age at menarche	2002	12.9	1.5	86	14.1	1.7	677	13.4	1.5	344	12.8	1.3	292	12.4	1.4	337	12.4	1.4	266	12.2	1.5	<0.001
Age at menopause	879	51.4	3.5	80	50.9	4.3	576	51.7	3.5	223	50.9	2.8	—	—	—	—	—	—	—	—	—	0.18
Age at first birth	1178	26.4	3.5	82	26.3	3.8	606	26.1	3.4	283	26.5	3.4	207	27.0	3.9	—	—	—	—	—	—	0.003
Height	2002	156.5	5.5	86	151.8	5.5	677	154.6	4.8	344	156.4	5.0	292	158.4	5.3	337	158.9	5.5	266	158.0	5.6	<0.001

Age is calculated at the end of 2008.

in or before 1968, the age at first birth was higher than in younger subjects. In addition, the parity was lower in younger subjects.

The mean height of subjects who were born in or around 1938 was ~152 cm (Table 2). For subjects who were born in or around 1984, the mean height was ~158 cm. Height

was greater in younger subjects but this trend reaches a plateau.

In each age group, ~10% of the subjects reported the premenopausal use of oral contraceptives (Table 3). The percentage was slightly higher in subjects who were born between 1959 and 1988 compared with older age groups. More than 40% of the subjects who used oral contraceptives used them for 3 months or less. However, 8.6% used oral contraceptives for 3 years or more. More than 10% of postmenopausal subjects aged 50 years or older reported the postmenopausal use of hormones.

Alcohol consumption was investigated using the three-status method: present, previously present (current status: abstinence from alcohol) and absent. Of the subjects, 50.7% reported currently consuming alcohol. The proportion of subjects consuming alcohol was higher in younger subjects (P value for trend <0.001) (Table 3).

Concerning family history, the proportion of subjects with a one relative with breast cancer is $<10\%$ for all ages. The proportion of subjects with two or more relatives diagnosed with breast cancer is very low and the proportion was not increasing with respect to birth year (Table 3).

DISCUSSION

This study showed the prevalence of breast cancer risk factors in Japan. With respect to age, in younger subjects, the age at menarche was lower, the age at the first delivery was higher, the parity was lower, the proportion of subjects utilizing hormones before menopause was slightly higher, the height was higher and the proportion of subjects

consuming alcohol was higher. Although the proportion of persons with a family history of breast cancer is still low, it will increase along with a rise in breast cancer incidence in the near future. In addition to that, the younger age group will have more chance to have a family history in her future.

In this study, an Internet survey was employed for the following reasons: nationwide data are available, and subjects do not hesitate to answer questions regarding delicate issues including reproductive health because of its anonymous nature. If the validity of Internet surveys is confirmed, changes in the prevalence of risk factors and scores can be investigated longitudinally via serial surveys. To examine the validity and the reproducibility of the results, the results for height and alcohol consumption were compared with those from the National Health and Nutrition Survey conducted in the same fiscal year (15). The mean height and its trend across age groups were very similar to those from the National Health and Nutrition Survey: 157.9 cm for age 20–29, 158.0 cm for age 30–39, 157.5 cm for age 40–49, 154.5 cm for age 50–59, 151.9 cm for age 60–69 and 147.4 cm for age 70 and over. As for alcohol consumption, proportions of present drinker (more than or equal to once a month) are 46.1% for age 20–29, 43.2% for age 30–39, 47.4% for age 40–49, 36.2% for age 50–59, 24.5% for age 60–69 and 14.7% for age 70 and over in that survey and these figures were lower than ours but trend across age groups was very similar. The National Health and Nutrition Survey was conducted using different sampling scheme from ours; the sample size for female subjects was 4140, twice as large as our study and the response rate was 59.1% from stratified random-sampled areas. The consistency of the

Table 3. Prevalence of breast cancer risk factors by birth year in Japanese women

	Total (<i>n</i> = 2002)	≤1938 (age ≥70) (<i>n</i> = 86)	1939–1948 (age 60–69) (<i>n</i> = 677)	1949–1958 (age 50–59) (<i>n</i> = 344)	1959–1968 (age 40–49) (<i>n</i> = 292)	1969–1978 (age 30–39) (<i>n</i> = 337)	1979–1988 (age 20–29) (<i>n</i> = 266)	<i>P</i> for trend
Parity >0 (%)	1423 (71.1)	82 (95.3)	606 (89.5)	283 (82.3)	207 (70.9)	190 (56.4)	55 (20.7)	<0.001
Oral contraceptives use (%)	243 (12.1)	1 (1.2)	69 (10.2)	36 (10.5)	41 (14.0)	57 (16.9)	39 (14.7)	<0.001
Postmenopausal hormone replacement therapy (%) ^a	122 (12.0)	3 (3.5)	89 (13.3)	30 (11.6)	—	—	—	0.28
Alcohol consumption (%)								
Present	1015 (50.7)	30 (34.9)	312 (46.1)	185 (53.8)	162 (55.5)	177 (52.5)	149 (56.0)	<0.001
Previously present	83 (4.1)	3 (3.5)	23 (3.4)	10 (2.9)	9 (3.1)	20 (5.9)	18 (6.8)	
Absent	904 (45.2)	53 (61.6)	342 (50.5)	149 (43.3)	121 (41.4)	140 (41.5)	99 (37.2)	
No. of relatives who have family history of breast cancer (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
0	1956 (97.7)	83 (96.5)	650 (96.0)	335 (97.4)	287 (98.3)	336 (99.7)	265 (99.6)	<0.001
1	39 (1.9)	3 (3.5)	21 (3.1)	8 (2.3)	5 (1.7)	1 (0.3)	1 (0.4)	
2	6 (0.3)	0 (0.0)	5 (0.7)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	
>2	1 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

^aDenominator of percent subjects for postmenopausal hormone replacement therapy is 1013 for total, 86 for age 70, 669 for age 60–69 and 258 for age 50–59. Data are not shown for age 20–49 due to small numbers. Age is calculated at the end of 2008.

results, especially trends across age groups, from studies with different sampling schemes was the supportive evidence of the reproducibility of the results, although the subjects in both studies were not sampled randomly from the population. If the risk of breast cancer in Internet users was higher than in non-Internet users, for example, due to an advanced education level and delayed initial childbirth, the risk factor trends observed in this study can be generalized if higher risk of Internet users is observed regardless of age (no interaction with cohort effect). More extremely, if the interaction existed, where Internet users tended to have delayed initial childbirth related to higher education in the older age group but no difference in the younger age group, this selection bias would work toward diminishing trends across age groups. We might observe stronger trends if no selection bias existed.

Since the study was a cross-sectional questionnaire survey, trend across age groups may not be a cohort effect but an age effect. For example, recall of past hormone use or age at menarche may be different by age. In this study, the inability to recall old memories may cause non-differential misclassification rather than differential misclassification. In other words, errors may be related to precision not related to accuracy. In that case, trend across age would diminish and the observed trend may not be caused by the recall bias. The factors not observed trend across age groups such as past hormone use and age at menopause may show trend if more precise measurements were used.

Based on the results, the number of women with each risk factor for breast cancer has increased, so that the incidence of breast cancer in Japanese women may be increasing over the next few decades. However, most of these factors are impossible to modify. High-risk females should more actively adopt strategies to prevent breast cancer and undergo screening. Furthermore, alcohol consumption can be modified; therefore, abstention from alcohol may be more prominently included in efforts to prevent breast cancer.

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Conflict of interest statement

None declared.

References

1. International Agency for Research on Cancer. Globocan 2002. <http://www-dep.iarc.fr/> (6 August 2012, date last accessed).
2. Center for Cancer Control and Information Services, National Cancer Center, Japan. <http://ganjoho.jp/professional/statistics/statistics.html> (6 August 2012, date last accessed).
3. World Cancer Research Fund/American Institute for Cancer Research. *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective*. Washington, DC: AICR 2007.
4. Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center. Evaluation of evidence. http://epi.ncc.go.jp/can_prev/ (6 August 2012, date last accessed).
5. Hayashi K, Mizunuma H, Fujita T, et al. Design of the Japan Nurses' Health Study: a prospective occupational cohort study of women's health in Japan. *Ind Health* 2007;45:679–86.
6. Ministry of Health, Labour, and Welfare. Outline of Results from 2008 National Health and Nutrition Survey. http://www.mhlw.go.jp/english/wp/wp-hw4/dl/health_and_medical_services/P65.pdf (6 August 2012, date last accessed).
7. Gail MH, Brinton LA, Byar DP, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst* 1989;81:1879–86.
8. Couper MP. Web surveys: a review of issues and approaches. *Public Opin Q* 2000;64:464–94.
9. Schmidt WC. World-Wide Web survey research: benefits, potential problems, and solutions. *Behav Res Meth Instrum Comput* 1997;29:274–9.
10. Kraut R, Olson J, Banaji M, Bruckman A, Cohen J, Couper M. Psychological research online: report of Board of Scientific Affairs' Advisory Group on the Conduct of Research on the Internet. *Am Psychol* 2004;59:105–17.
11. Rhodes SD, Bowie DA, Hergenrather KC. Collecting behavioural data using the world wide web: considerations for researchers. *J Epidemiol Community Health* 2003;57:68–73.
12. Yasunaga H, Ide H, Imamura T, Ohe K. Medical research using Internet questionnaire in Japan. *Nippon Koshu Eisei Zasshi* 2006;53:40–50 (in Japanese).
13. Couper MP. Issues of representation in eHealth research (with a focus on web surveys). *Am J Prev Med* 2007;32:S83–9.
14. Im EO, Chee W. Issues in internet survey research among cancer patients. *Cancer Nurs* 2004;27:34–44.
15. Ministry of Health, Labour, and Welfare. Report of 2007 National Health and Nutrition Survey. <http://www.mhlw.go.jp/bunya/kenkou/eiyoun09/01.html> (6 August 2012, date last accessed).

Physicians' knowledge, attitude, and behavior regarding fertility issues for young breast cancer patients: a national survey for breast care specialists

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Abstract

Background Fertility is one of the key aspects of quality of life for breast cancer patients of childbearing age. The objective of this study was to describe fertility-related practice for young breast cancer patients in Japan and to identify healthcare provider factors that contribute to physicians' behavior towards fertility preservation.

Methods A cross-sectional survey was developed in order for Japanese breast cancer specialists ($n = 843$) to self-evaluate their knowledge, attitude, and behavior regarding fertility preservation. Survey items included questions regarding knowledge of and attitude toward fertility issues in cancer patients, fertility-related practice, potential barriers for the discussion of fertility with patients, and responding physicians' socio-demographic background.

Results Four hundred and thirty-four (52%) breast oncologists responded to the survey. Female and younger oncologists (age less than 50 years) had significantly higher probability of referring patients to reproductive

specialists. Physicians who had better knowledge score and positive attitudes toward fertility preservation were more likely to discuss potential fertility issues with cancer patients. This was significantly associated with consultation and referral to reproduction specialists when encountering fertility issues with cancer patients. Risk of recurrence, lack of collaborating reproductive specialists, and time constraints in the clinic were identified as major barriers to discussion of fertility preservation with breast cancer patients.

Conclusion Female and younger physicians as well as physicians working in a multidisciplinary environment had positive attitudes and behavior towards fertility preservation in breast cancer patients. The development of comprehensive and interdisciplinary programs for healthcare providers is necessary to meet the expectations and fertility needs of breast cancer patients.

Keywords Fertility preservation · Breast cancer · Survivorship

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Introduction

With improvement of cancer prognosis, fertility has become one of the key aspects of quality of life for breast cancer patients of childbearing age. Distress about interrupted childbearing is likely to persist in long-term female cancer survivors [1]. The American Society of Clinical Oncology (ASCO) has developed guidance for oncologists regarding available fertility preservation methods and related issues [2]: oncologists should address the possibility of infertility with patients during their reproductive years and be prepared to discuss possible fertility preservation options or refer appropriate and interested patients to

reproductive specialists as early as possible during treatment planning.

However, previous studies have shown that only 23% of the patients younger than 40 years of age were informed of potential infertility after cancer treatment in a single institution in Japan and less than half of oncologists were following the ASCO guideline in the USA [3, 4]. The practice of oncologists regarding fertility preservation in cancer patients of reproductive age may depend on multiple factors: the patient's medical and psychosocial condition [5, 6], the patient's knowledge [7], and physicians' knowledge about fertility preservation [8].

We have previously analyzed the decision-making process for adjuvant treatment in young breast cancer patients of reproductive age [3]. Significantly less patients expressed interest in fertility when they had children or advanced disease. Less aggressive treatment (without chemotherapy) was recommended by oncologists for patients who voluntarily expressed an interest in preserving fertility [3]. Nearly one-third of the patients who expressed an interest in fertility selected a different adjuvant treatment from the primary recommendation of the oncologist because of their concern for preserving fertility, whereas the majority of patients who did not express an interest in preserving fertility followed the oncologists' primary recommendation [3].

The awareness and attitude of patients in the clinic might reflect the ability of healthcare providers to provide an environment in which patients could bring up fertility issues. The objectives of this study include describing fertility-related practice for breast cancer patients in a variety of clinical settings in Japan and identifying healthcare provider factors that contribute to physicians' behavior regarding fertility preservation in young breast cancer patients.

Methods

Selection of participant

A cross-sectional survey was developed in order for board-certified breast oncologists of the Japanese Breast Cancer Society (JBCS), who are the main physicians treating breast cancer patients in Japan, to self-evaluate their knowledge, perception, and behavior regarding fertility issues in young breast cancer patients.

Measures

The survey consisted of 49 items including questions regarding knowledge of and attitudes towards fertility in cancer patients, practice behavior of fertility-related discussions with patients, potential barriers for these

discussions, and demographic background of the practitioners (Table 1). Survey items were derived from existing literature and multidisciplinary discussion. Physicians were asked to evaluate their agreement with the statements using a five-grade system (1, strongly agree; 2, agree; 3, cannot decide; 4, disagree; 5, strongly disagree).

1. Knowledge about fertility issues in breast cancer patients

To evaluate the accuracy of knowledge about fertility issues in breast cancer patients, the statements were developed from the latest JBCS treatment guideline [5]. For statements A-1 and A-4, the respondents were considered to have more accurate knowledge when the score was lower. For statements A-2 and A-3, the respondents were considered to have more accurate knowledge when the score was higher. Then the sum of $(5 - \text{"score for A-1"}) + (\text{"score for A-2"}) + (\text{"score for A-3"}) + (5 - \text{"score for A-4"})$ was calculated. The respondents with a higher sum were considered to have more accurate overall knowledge. A-5 was not used to evaluate the accuracy of knowledge because of lack of definite evidence, but correlated with the use of LHRH agonist for fertility preservation.

2. Practice behavior for breast cancer patients of reproductive age

Practice behavior statements consisted of 13 items including statements used in the US oncologist survey with some modifications to adapt to Japanese practice setting. The statements "I discuss the impact of cancer treatment on future fertility with my patients", "I consult reproductive specialists with questions about fertility issues in my patients", and "I refer patients who have questions about fertility to reproductive specialists" were considered the most important behavior according to the ASCO guideline [2].

3. Potential barriers for discussing fertility issues with breast cancer patients

Among seven potential barriers asked in the questionnaire, four were similar to statements used in the US survey [4]. We put three additional statements (patients' voluntary expression of interest, existence of spouse/partner, and support from co-medical staff) that were created by findings from our previous study [2] and by considering Japanese culture. In addition, we asked the participant to describe the greatest difficulty in discussing fertility in an open question.

4. Attitude towards fertility preservation of cancer patients

Five statements were selected from the US survey [4]. Because the hereditary aspect of breast cancer was considered to be not genuinely linked with perception of

Table 1 Questionnaire statements

- A. Knowledge about fertility issues of breast cancer patients**
1. Total dose of alkylating agents are related to infertility
 2. Pregnancy after breast cancer increases risk of recurrence
 3. Pregnancy after chemotherapy increases risk of deformity of the child
 4. Pregnancy should be avoided during tamoxifen treatment
 5. Luteinizing hormone releasing hormone (LHRH) analogue reduces the risk of chemotherapy-induced amenorrhea
- B. Practice behavior**
1. Patients voluntarily bring up the fertility issues in the clinic
 2. I discuss the impact of cancer treatment to future fertility with my patients
 3. I do not feel comfortable to discuss fertility issue with my patients
 4. I take into account the history of childbirth when I discuss fertility issue with my patient
 5. I take into account whether she has a spouse/partner when I discuss fertility issue with my patient
 6. I take into account economical status of the patient when I discuss fertility issue with my patient
 7. I discuss fertility issues with breast cancer patients with high risk of recurrence
 8. Patients talk to co-medical staff about their concern about fertility
 9. I ask co-medical staff if a patient has an interest in fertility
 10. I provide my patients with educational material about fertility preservation
 11. I use LHRH analogue to preserve fertility
 12. I consult a reproductive specialist with questions about fertility issues in my patients
 13. I refer patients who have questions about fertility to reproductive specialists
- C. Barriers for discussing fertility issues**
1. The patient does not express their interest in fertility
 2. The patient has high risk of recurrence
 3. The patient has economic problems
 4. The patient does not have a spouse/partner
 5. There is no place/person to refer my patients to for fertility preservation
 6. Time constraints affect my ability to discuss fertility preservation
 7. There is no support from co-medical staff
 8. What is the greatest difficulty in discussing fertility issues with young breast cancer patients?
- D. Attitude toward fertility preservation**
1. Patients with poor prognosis should not pursue fertility preservation
 2. Posthumous parenting is troublesome for bereaved family
 3. Losing mothers will negatively affect bereaved children
 4. I fear passing hereditary cancer to a biological child
 5. Treating cancer is more important than fertility preservation
- E. Demographics and medical backgrounds**
1. What is your gender?

Table 1 continued

2. What is your age?
3. What is your religious background?
4. When did you graduate from medical school?
5. What is your specialty?
6. Where is your primary practice located?
7. What kind of institution do you practice in?
8. Is your institution a community-base hospital for cancer care?
9. How many physicians are in your practice setting including you?
10. Are there any female physicians in your practice setting?
11. Are there any medical oncologists in your practice setting?
12. Are there any breast cancer specialized nurses in your practice setting?
13. Are there any cancer-specialized pharmacists in your practice setting?
14. Is there a genetic counseling clinic in your practice setting?
15. In a typical week, how many breast cancer surgeries are performed in your practice setting?
16. In a typical week, how many breast cancer patients under 40 years of age do you see?
17. Do you have a spouse/partner?
18. Do you have children?
19. Do you have relatives or close friends who passed away leaving behind minor children?

fertility preservation, the item was not included in our analysis. Participants were considered to be positive toward fertility preservation if the sum of scores was higher than 3. The sum of scores for statements from D-1 through D-5 was calculated and the respondents with higher total score were considered as physicians with a “positive attitude” towards fertility preservation.

5. Individual and institutional background

The items included physicians’ gender, age, religious background, length of professional career, and specialty. We also asked for a description of the practicing institution: the number of breast surgeries, the number of young breast cancer patients, presence of female colleagues in the team, the presence of one or more medical oncologist(s), breast cancer certified clinical nurse specialist (CNS), and board-certified pharmacists in the institution.

Procedures

The study was carried out according to the National Guideline for Epidemiological Studies. The names of study participants and the institutions of breast oncologists were obtained from the JBCS website. After confirmation of each physician’s affiliation, anonymous paper surveys were sent out to all 843 breast oncologists by mail with a return

postage-paid envelope. The survey was sent out on 28 May 2010 and the mailed surveys postmarked by 31 July were included in the analysis. The consent from the participants was waived because of the anonymity of the survey. No honorarium was offered for completing the survey.

Data analysis

All analyses were conducted using IBM SPSS statistics version 18. Accuracy of knowledge about fertility was scored on the basis of four questions (A-1, 2, 3, 4, Table 1) concerning the standard knowledge about chemotherapy and the effect of chemotherapy on fertility. Respondents with appropriate knowledge were considered “accurate”. Four questions (D-1, 2, 3, 5, Table 1) concerning the perspective and opinion about the fertility preservation were asked and scored as attitude score. Respondents were divided into “positive attitude group” and “negative attitude group” depending on the attitude score. Chi-square test was applied for correlation analysis between physician knowledge, attitude, and background. Physicians’ background demographics, knowledge, and attitude regarding fertility issues were associated with physicians’ practice behavior regarding fertility issues. Odds ratios (OR) and their 95% confidence interval (CI) were estimated to compare physician background factors, knowledge, and attitude with physician practice pattern, using simple and multivariable logistic regression models. All *p* values are two sided, and the statistical significance level was set at $p < 0.05$. No adjustments for multiple comparisons were considered because of the exploratory nature of this study.

Results

Response rate

The response rate was calculated as the number of breast oncologists completing the survey ($n = 434$) divided by the initial sample size minus undeliverable ($843 - 8 = 835$): this yielded a 52% response rate. This is higher than the previous survey on fertility preservation referral targeting oncology specialists in the USA [4].

Demographic and characteristics of responding breast oncologists

The background of respondents is shown in Table 2. A total of 16.6% of the respondents were female. More than 95% of the respondents were experienced physicians reflecting the requirement of basic board certification in general medicine, surgery, radiation oncology, or pathology in order to obtain JBCS Breast Oncologists

certification. The majority was surgeons. Less than half responded that they have medical oncologists in their institutions. About 70% were the institutions in which they operated on less than five breast cancer patients per week (less than approximately 200 cases per year).

Association between knowledge, attitude, and physician background

Two hundred and seventy-nine (64%) respondents were considered to have accurate knowledge. Accuracy of knowledge about fertility was correlated with the number of young breast cancer patients treated ($p = 0.006$), presence of children of the physician ($p = 0.01$), age of the physician ($p = 0.019$), and the presence of female colleagues ($p = 0.019$).

The existence of a spouse/partner ($p = 0.011$), age ($p = 0.032$), and gender ($p = 0.023$) of the physician were the factors significantly correlated with a positive attitude toward fertility considerations of breast cancer patients. Physicians who have a spouse/partner, physicians who are younger than 50 years, and female physicians had more positive attitudes toward fertility issues for breast cancer patients.

Practice of fertility issues among breast oncologists

A total of 83% of the participants responded that they were positive in discussing fertility issues with young breast cancer patients.

Twenty-one percent responded that patients voluntarily bring up fertility issues in the clinic. Physicians who treat two or more young patients per week perceived that patients voluntarily express their concern in the clinic compared to physicians who treat fewer (OR 1.84, 95% CI 1.13–3.00, $p = 0.008$). Physicians who treat two or more young patients per week (OR 1.30, 95% CI 1.05–2.45, $p = 0.023$), who have board-certified nurse colleagues (OR 1.55, 1.19–2.03, $p < 0.001$) and have more than six breast surgeries per week (OR 1.20, 1.02–1.41, $p = 0.014$) responded that they perceived that patients talk to co-medical staff about their concerns about fertility. A total of 24% of the respondents consulted reproductive specialists when they encountered fertility problems in their patients and 42% referred patients to reproductive specialists when patients expressed concerns regarding fertility.

The association between physicians’ behavior related to fertility issues and their knowledge, attitude, and background demographics are shown in Table 3. Fair knowledge had the strongest impact on physicians’ positive behavior towards discussing fertility issue with patients. Positive attitude, presence of breast cancer-specialized CNS, young age, and female gender were also significant

Table 2 Demographic background of the responding physicians

	<i>n</i>	%
Total	434	100
Gender		
Female	72	16.6
Male	357	82.3
Unknown	5	1.2
Age		
20–29	1	0.2
30–39	52	12.0
40–49	183	42.2
50–59	148	34.1
60–69	41	9.4
70–	4	0.9
Unknown	5	1.2
Religion		
Buddhist	144	33.2
Christian	9	2.1
No special religion	276	63.5
Others	5	1.2
Year graduated from medical school		
–1994	347	80.0
1995–2000	76	17.5
2001–2005	6	1.4
Unknown	5	1.2
Specialty		
Surgery	412	94.9
Medical oncology	6	1.4
Radiation oncology	9	2.1
Gynecology	1	0.2
Others	6	1.4
Type of affiliation		
Cancer center	40	9.2
General hospital	190	43.8
University hospital	122	28.1
Private clinic	74	17.1
Unknown	8	1.8
Number of physicians		
1–3	164	37.8
4–7	137	31.8
8–	125	28.8
Unknown	8	1.8
Female physician colleague		
Present	276	63.6
Absent	150	34.6
Unknown	8	1.8
Medical oncologist		
Present	172	39.6
Absent	255	58.8
Unknown	7	1.6

Table 2 continued

	<i>n</i>	%
Breast cancer specialized nurse		
Present	202	46.5
Absent	225	51.8
Unknown	7	1.6
Board-certified pharmacists		
Present	227	52.3
Absent	196	45.2
Unknown	11	2.5
Number of breast surgeries (per week)		
0–5	310	71.4
5–10	85	19.5
11–15	14	3.2
16–20	3	0.7
20–	14	3.2
Unknown	8	1.8
Number of patients aged <40 (per week)		
0–1	122	28.1
2–4	202	46.5
5–	103	23.7
Partner/spouse		
Present	401	92.4
Absent	25	5.8
Unknown	8	1.8
Children		
Present	351	80.9
Absent	64	14.7
Unknown	19	4.4

factors associated with positivity towards the discussion. Female oncologists and medical oncologists were more likely to take into account patients' social backgrounds such as history of childbirth, presence of a spouse/partner, and patients' economic status when discussing fertility issues.

Physicians with a positive attitude, physicians younger than 50 years, and female physicians were more likely to discuss fertility issues with patients with poorer prognoses. Positive attitude was the strongest factor related to consultation and referral to reproductive specialists.

Barriers for discussion with patients

High risk of disease recurrence (51%), lack of reproductive specialists or infertility clinic for referral (45%), and time constraints in the clinic (45%) were regarded as major barriers for discussing fertility issues. When only physicians who were negative in discussing fertility issues ($n = 69$) were analyzed, high risk of recurrence (57%), no signal of interest in fertility from patients (49%), and lack

Table 3 Factors associated with fertility-related practice behavior

	I discuss the impact of cancer treatment on future fertility with my patients				I do not feel comfortable discussing fertility issues with my patients				I take into account the history of childbirth when I discuss fertility issues with my patients			
	<i>p</i>	OR	95% CI		<i>p</i>	OR	95% CI		<i>p</i>	OR	95% CI	
			Min	Max			Min	Max			Min	Max
Knowledge												
Fair	0.000	1.717	1.321	2.231	0.063				0.799			
Not fair		1.000										
Attitude												
Conservative	0.012	1.000			0.180				0.697			
Aggressive		1.542	1.145	2.079								
Gender												
Female	0.005	1.166	1.080	1.258	0.807				0.022	1.130	1.041	1.227
Male		1.000								1.000		
Age												
<50	0.000	1.584	1.280	1.959	0.203				0.625			
>50		1.000										
Specialty												
Surgery	1.000				0.625				0.756			
Others												
Affiliation												
University hospital/cancer center	0.032	1.235	1.047	1.457	0.147				0.900			
General hospital/private hospital		1.000										
Female physician colleague												
Present	0.079				1.000				1.000			
Absent												
Medical oncologist colleague												
Present	0.432				0.366				0.043	1.190	1.003	1.141
Absent												
Breast cancer-specialized nurse												
Present	0.606				0.480				0.327			
Absent												
Board-certified cancer pharmacist												
Present	0.001	1.510	1.220	1.868	0.721				0.324			
Absent		1.000										
Number of breast surgeries per week												
1–5	0.884				0.692				0.495			
6–												
Number of young patients per week												
0–1	0.474				0.113				0.500			
2–												
Partner/spouse												
Present	0.281				0.008	1.000			0.193			
Absent						1.158	0.989	1.355				
Children												
Present	0.074				0.088				0.740			
Absent												