Post-normal screen breast cancer in the Quebec breast cancer screening program (PQDCS)

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Abstract

Background: Interval breast cancer is a mix of false-negative and incident cases susceptible to compromise the mortality reduction targeted by screening programs.

Objectives: Evaluate clinical features and risk factors for post-normal screen breast cancer by period of diagnosis.

Methods: We used a case-control design to compare all women with screen-detected (n=1 699) or post-normal screen breast cancer (n=711) and a random sample of 48 200 normal controls, matched for trimester of mammography, selected among first participants to the PQDCS between 1998 and 2000. Data from the information system were linked with the Quebec hospital discharge and Medicare databases and pathology reports. Mammograms were not independently reviewed. Data were analysed by logistic regression, correcting for intra-radiologist and intra-clinic correlations.

Results: Incidence of post-normal screen cancer went from 7.1 to 19.9 and 33.4/10 000 person-years at 0-12, 13-24 and 25-36 months after mammography. Interval tumours were more often invasive than screen-detected ones (92% vs 79%), large (mean: 2.0 vs 1.4 cm), node-positive (41.6% vs 25.2%) and high grade (33.6% vs 14.4%). Clinical features varied according to period of diagnosis, as did several associations with risk factors for breast cancer. This was most notable for breast density (odds ratio (OR) for > 75% vs < 25%; 13.0 (95% confidence interval; 6.8.24.9), 3.3 (2.3.4.8) and 2.5 (1.1,5.7)), family history of breast cancer (OR: 1.3 (0.8,1.9), 2.5 (2.0,3.0) and 1.5 (1.0.2.2)) and body mass index (OR for \geq 35 vs < 20; 2.2 (0.8.6.3). 1.9 (1.1.3.2) and 0.9 (0.3.2.8)), at 0-12, 13-24 and 25-36 months after screening mammography.

Conclusions: Post-normal screen breast cancer is a group with adverse prognostic features. Analysis by interval since normal mammography highlights the interplay of masking effects and force of morbidity. Breast cancer incidence rapidly returns to pre-screening level in non compliant women.

Background

- The Quebec breast cancer screening program (PQDCS) is a population-based program with biennial mammography launched in 1998
- Target population: women 50-69 years old
- Participation follows formal invitation by letter or medical prescription
- Written consent to participate to the information system (SI-PQDCS) solicited
- Continuous normative evaluation

Objectives

- Estimate the frequency of post-normal screen breast cancer up to 36 months after a first participation to the PQDCS
- Describe clinical / pathological features and risk factors for these cases
- Compare them to women with screen-detected breast cancer and to normal controls

Materials and methods

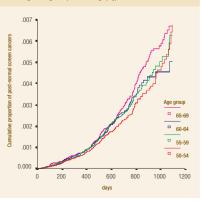
- . Design: case-control study
- Source population: first participants to the PQDCS between 1998 and 2000
- Study population: all women with screen-detected breast cancer (n=1 699). interval breast cancer diagnosed within 36 months after a normal / benign screening mammogram (n=711), and a random sample of healthy women with normal mammography (n=48 200)
- Sources of information: SI-PQDCS and review of pathology reports
- Data analysis: logistic regression models including all characteristics of women, radiologists and screening centres, with correction for intra-radiologist and intra-clinic correlations

Results

Incidence of post-normal screen breast cancer (first mammography) - PQDCS 1998-2000

	MO	MONTHS BETWEEN SCREENING AND DIAGNOSIS						
	≤ 36	≤ 12	13-24	25-36				
ALL TUMOURS (/10 000 py.)								
50-54 55-59 60-64 65-69 50-69	12.9 14.6 14.5 17.7 14.6	6.3 7.4 7.8 7.5 7.1	17.6 20.0 20.0 24.3 19.9	33.1 33.6 30.1 35.9 33.4				
(/10 000 py.)	ONLY							
50-54 55-59 60-64 65-69 50-69	11.5 13.4 13.6 15.2 13.1	5.7 7.1 7.1 6.1 6.4	15.3 18.2 19.1 21.6 18.0	29.8 29.3 27.7 29.7 29.3				

Occurrence of post-normal screen breast cancer by age and interval between screening and diagnosis (first mammography) - PQDCS 1998-2000



CHARACTERISTICS OF SCREEN-DETECTED AND POST-NORMAL SCREEN BREAST TUMOURS (FIRST MAMMOGRAPHY)- PODCS 1998-2000.

	SCREEN-DETECTED CANCER	POST-NORMAL SCREEN CANCER MONTHS RETWEEN SCREENING AND DIAGNOSIS								
	OFFICE	NOSIS								
	n=1 699	≤ 36 n=711	≤ 12 n=165	13-24 n=404	25-36 n=142					
Invasiveness invasive in situ unknown	1 307 (79.0) 348 (21.0) 44	641 (92.0) 56 (8.0) 14	150 (94.9) 8 (5.1) 7	365 (91.7) 33 (8.3) 6	126 (89.4 15 (10.6					
Characteristics of	invasive tumours									
Average size (cm)	1.39	2.04	2.30	1.98	1.99					
No. invaded node: 0 1-3 4+ unknown *	700 (74.8) 175 (18.7) 61 (6.5) 371	265 (58.4) 120 (26.4) 69 (15.2) 187	37 (48.7) 21 (27.6) 18 (23.7) 74	164 (59.9) 71 (25.9) 39 (14.2) 91	64 (61.5 28 (26.9 12 (11.5 22					
Histological type ductal lobular tubular other unknown	917 (78.6) 103 (8.8) 84 (7.2) 63 (5.4) 140	382 (76.1) 74 (14.7) 16 (3.2) 30 (6.0) 139	65 (73.9) 17 (19.3) 3 (3.4) 3 (3.4) 62	238 (78.6) 37 (12.2) 7 (2.3) 21 (6.9) 62	79 (71.2 20 (18.0 6 (5.4 6 (5.4					
Tumour grade I II III unknown		121 (27.6) 170 (38.8) 147 (33.6) 203	20 (27.0) 26 (35.1) 28 (37.8) 76	72 (27.2) 105 (39.6) 88 (33.2) 100	29 (29.3 39 (39.4 31 (31.3 27					
Lymphatic-vascul present absent unknown	177 (20.7) 680 (79.3) 450	162 (38.6) 258 (61.4) 221	30 (42.9) 40 (57.1) 80	102 (40.3) 151 (59.7) 112	30 (30.9 67 (69.1 29					
* Includes cases with missing information and without node dissection										

DISTRIBUTION OF WOMEN WITH SCREEN-DETECTED BREAST CANCER, POST-NORMAL SCREEN

POST-NORMAL SCREEN CANCER

	CANCER	MONTHS BETWEEN SCREENING AND DIAGNOSIS						
		≤ 36	≤ 12	13-24	25-36			
	n=1 699 (%)	n=711 (%)	n=165 (%)	n=404 (%)	n=142 (%)	n=48 200 (%)		
Age	59.5 ± 5.9	59.3 ± 5.9	59.2 ± 5.7	59.1 ± 5.8	59.9 ± 6.4	58.4 ± 5.7		
Number of children	2.7 ± 1.5	2.7 ± 1.6	2.7 ± 1.4	2.7 ± 1.6	2.8 ± 1.5	2.7 ± 1.5		
Age at 1st childbirth	24.6 ± 4.7	24.7 ± 4.7	24.1 ± 4.1	24.9 ± 4.9	25.1 ± 4.6	23.9 ± 4.4		
Age at menopause	47.6 ± 6.0	48.0 ± 5.7	47.7 ± 6.2	48.2 ± 5.6	48.0 ± 5.6	47.0 ± 6.2		
BMI (kg/m²)	26.7 ± 5.0	25.5 ± 4.6	25.1 ± 4.2	25.7 ± 4.8	25.4 ± 4.5	26.2 ± 5.1		
Post-menopausal	1 518 (89.3)	642 (90.3)	150 (90.9)	366 (90.6)	126 (88.7)	42 506 (88.2)		
With family history of breast cancer	292 (17.2)	177 (24.9)	29 (17.6)	117 (29.0)	31 (21.8)	6 583 (13.7)		
Users of HRT	821 (48.3)	447 (62.9)	103 (62.4)	257 (63.6)	87 (61.3)	24 697 (51.2)		
Previous mammography	1 394 (82.0)	655 (92.1)	151 (91.5)	371 (91.8)	133 (93.7)	42 689 (88.6)		
Previous breast clinical examination	1 138 (67.0)	528 (74.3)	118 (71.5)	307 (76.0)	103 (72.5)	34 582 (71.7)		
Previous breast aspiration / biopsy	204 (12.0)	108 (15.2)	28 (17.0)	61 (15.1)	19 (13.4)	4 185 (8.7)		
Previous breast reduction	25 (1.5)	13 (1.8)	3 (1.8)	7 (1.7)	3 (2.1)	1 408 (2.9)		
8reast density <25% 25-49% 50-75% >75%			14 (8.5) 48 (29.1) 76 (46.1) 27 (16.4)	77 (19.1) 121 (29.9) 154 (38.1) 52 (12.9)	19 (13.4) 60 (42.3) 53 (37.3) 10 (7.0)	15 754 (32.7) 17 536 (36.4) 11 881 (24.7) 3 029 (6.3)		

ASSOCIATIONS OF SCREEN-DETECTED AND POST-NORMAL SCREEN BREAST CANCER WITH CHARACTERISTICS OF WOMEN (FIRST MAMMOGRAPHY) - PQDCS 1998-2000

		SCREEN-DETECTED CANCER (n=1 699)			POST-NORMAL SCREEN CANCER (n= 711)				
		OR			OR				
		crude	adj.	(95% c.i.)	crude	adj.	(95% c.i.)		
Age	50-54 55-59 60-64 65-69	1.00 1.20 1.41 1.66	1.00 1.29 1.53 1.77	(1.13-1.47) (1.32-1.77) (1.53-2.04)	1.00 1.15 1.09 1.41	1.00 1.18 1.23 1.77	(0.97-1.44) (0.98-1.53) (1.42-2.20)		
Age at 1 st childbirth	nulliparous < 20 20-24 25-29 30-34 ≥ 35	1.00 0.58 0.60 0.73 0.91 0.90	1.00 0.64 0.64 0.78 0.96 0.91	(0.53-0.78) (0.55-0.73) (0.67-0.91) (0.79-1.17) (0.66-1.24)	1.00 0.50 0.64 0.81 1.08 1.04	1.00 0.66 0.75 0.92 1.21 1.11	(0.48-0.91) (0.61-0.93) (0.73-1.16) (0.90-1.62) (0.71-1.74)		
Menopausal status	pre-menop. post-menop.	1.00 1.13	1.00 1.03	(0.86-1.23)	1.00 1.22	1.00 1.05	(0.80-1.36)		
Family history of breast cancer	no yes	1.00 1.34	1.00 1.30	(1.14-1.49)	1.00 2.02	1.00 1.93	(1.63-2.28)		
Use of HRT	never former current	1.00 0.88 0.88	1.00 0.88 0.99	(0.72-1.07) (0.88-1.11)	1.00 0.75 1.52	1.00 0.74 1.43	(0.51-1.07) (1.21-1.70)		
BMI (kg/m²)	< 20.0 20.0-24.9 25.0-29.9 30.0-34.9 ≥ 35.0	1.00 1.20 1.37 1.46 1.47	1.00 1.33 1.66 1.93 2.19	(1.08-1.64) (1.34-2.06) (1.54-2.42) (1.62-2.96)	1.00 0.91 0.72 0.61 0.68	1.00 1.12 1.10 1.18 1.63	(0.84-1.50) (0.82-1.49) (0.84-1.65) (1.02-2.59)		
Breast density	< 25 % 25-49 % 50-75 % > 75 %	1.00 1.59 1.75 1.48	1.00 1.71 1.98 1.78	(1.49-1.96) (1.70-2.31) (1.41-2.23)	1.00 1.91 3.47 4.30	1.00 1.90 3.43 4.18	(1.49-2.42) (2.68-4.39) (3.08-5.66)		
Previous mammography	no yes	1.00 0.59	1.00 0.55	(0.48-0.64)	1.00 1.51	1.00 1.14	(0.87-1.49)		
Previous breast clinical examination	no yes	1.00 0.81	1.00 0.84	(0.75-0.94)	1.00 1.09	1.00 1.00	(0.85-1.19)		
Previous breast aspiration/ biopsy	no yes	1.00 1.45	1.00 1.41	(1.21-1.65)	1.00 1.84	1.00 1.50	(1.21-1.86)		
Previous breast reduction	no yes	1.00 0.49	1.00 0.55	(0.36-0.83)	1.00 0.62	1.00 0.78	(0.43-1.41)		

ASSOCIATIONS OF POST-NORMAL SCREEN BREAST CANCER WITH CHARACTERISTICS OF WOMEN. BY INTERVAL BETWEEN SCREENING AND DIAGNOSIS (FIRST MAMMOGRAPHY) - PODCS 1998-2000

MONTHS BETWEEN SCREENING AND DIAGNOSIS

oune	(n=1 699) (n=711)					≤ 12		13-24		-36			
	OR	}		OF	3				OR		0R	0	R
ide	adj.	(95% c.i.)	crude	adj.	(95% c.i.)			adj.	(95% c.i.)	adj.	(95% c.i.)	adj.	(95% c.i.)
00	1.00		1.00	1.00		Age	50-54	1.00		1.00		1.00	
20	1.29	(1.13-1.47)	1.15	1.18	(0.97-1.44)		55-59	1.31	(0.91-1.90)	1.14	(0.87-1.49)	1.19	(0.76-1 86)
41	1.53	(1.32-1.77)	1.09	1.23	(0.98-1.53)		60-64	1.61	(1.05-2.48)	1.16	(0.85-1.59)	1.01	(0.59-1.72)
66	1.77	(1.53-2.04)	1.41	1.77	(1.42-2.20)		65-69	1.75	(1.10-2.78)	1.64	(1.21-2.21)	2.13	(1.31-3.47)
00	1.00		1.00	1.00		Age at 1st	nulliparous	1.00		1.00		1.00	
58	0.64	(0.53-0.78)	0.50	0.66	(0.48-0.91)	childbirth	< 20	0.99	(0.54-1.83)	0.60	(0.39 - 0.93)	0.55	(0.27-1.10)
60	0.64	(0.55-0.73)	0.64	0.75	(0.61-0.93)		20-24	1.17	(0.77-1.78)	0.72	(0.54-0.95)	0.52	(0.33-0.83)
73	0.78	(0.67-0.91)	0.81	0.92	(0.73-1.16)		25-29	1.17	(0.74-1.86)	0.90	(0.66-1.22)	0.77	(0.47-1.27)
91	0.96	(0.79-1.17)	1.08	1.21	(0.90-1.62)		30-34	1.41	(0.80-2.49)	1.18	(0.81-1.71)	1.11	(0.58-2.09)
90	0.91	(0.66-1.24)	1.04	1.11	(0.71-1.74)		≥ 35	0.85	(0.27-2.72)	1.26	(0.73-2.19)	0.93	(0.32-2.65)
00	1.00		1.00	1.00		Menopausal	pre-menop.	1.00		1.00		1.00	
13	1.03	(0.86-1.23)	1.22	1.05	(0.80-1.36)	status	post-menop.	1.25	(0.73-2.14)	1.10	(0.78-1.53)	0.80	(0.45-1.43)
00	1.00		1.00	1.00		Family history	no	1.00		1.00		1.00	
34	1.30	(1.14-1.49)	2.02	1.93	(1.63-2.28)	of breast cancer	yes	1.26	(0.84-1.91)	2.45	(1.99-3.01)	1.46	(0.98-2.17)
00	1.00		1.00	1.00		Use of HRT	never	1.00		1.00		1.00	
38	0.88	(0.72-1.07)	0.75	0.74	(0.51-1.07)		former	0.65	(0.32-1.34)	0.55	(0.32-0.96)	1.37	(0.73-2.55)
88	0.99	(0.88-1.11)	1.52	1.43	(1.21-1.70)		current	1.18	(0.82-1.72)	1.49	(1.18-1.88)	1.57	(1.09-2.25)
00	1.00		1.00	1.00		BMI (kg/m²)	< 20.0	1.00		1.00		1.00	
20	1.33	(1.08-1.64)	0.91	1.12	(0.84-1.50)		20.0-24.9	1.69	(0.86-3.35)	1.20	(0.80-1.79)	0.74	(0.40-1.38)
37	1.66	(1.34-2.06)	0.72	1.10	(0.82-1.49)		25.0-29.9	1.93	(0.98-3.79)	1.04	(0.67-1.62)	0.84	(0.45-1.58)
46	1.93	(1.54-2.42)	0.61	1.18	(0.84-1.65)		30.0-34.9	1.23	(0.53-2.86)	1.35	(0.84-2.17)	0.85	(0.40-1.84)
47	2.19	(1.62-2.96)	0.68	1.63	(1.02-2.59)		≥ 35.0	2.20	(0.77-6.30)	1.85	(1.06-3.23)	0.92	(0.30-2.78)
00	1.00		1.00	1.00		Breast density	< 25 %	1.00		1.00		1.00	
59	1.71	(1.49-1.96)	1.91	1.90	(1.49-2.42)		25-49 %	3.19	(1.84-5.55)	1.41	(1.04-1.91)	2.97	(1.76-5.01)
75	1.98	(1.70-2.31)	3.47	3.43	(2.68-4.39)		50-75 %	8.16	(4,47-14,88)	2.58	(1.91-3.48)	3.62	(2.10-6.25)
48	1.78	(1.41-2.23)	4.30	4.18	(3.08-5.66)		> 75 %	13.00	(6.79-24.89)	3.29	(2.26-4.79)	2.49	(1.09-5.70)
00	1.00		1.00	1.00		Previous	no	1.00		1.00		1.00	
59	0.55	(0.48-0.64)	1.51	1.14	(0.87-1.49)	mammography	yes	1.05	(0.60-1.82)	1.07	(0.76-1.50)	1.60	(0.82-3.12)
00	1.00		1.00	1.00		Previous breast	no	1.00		1.00		1.00	
81	0.84	(0.75-0.94)	1.09	1.00	(0.85-1.19)	clinical examination	yes	0.93	(0.65-1.32)	1.11	(0.88-1.40)	0.86	(0.58-1.29)
00	1.00		1.00	1.00		Previous breast	no	1.00		1.00		1.00	
45	1.41	(1.21-1.65)	1.84	1.50	(1.21-1.86)	aspiration / biopsy	yes	1.64	(1.09-2.47)	1.52	(1.17-1.98)	1.29	(0.75-2.20)
00	1.00		1.00	1.00		Previous breast	no	1.00		1.00		1.00	
49	0.55	(0.36-0.83)	0.62	0.78	(0.43-1.41)	reduction	yes	0.89	(0.22-3.56)	0.69	(0.33-1.46)	0.98	(0.32-3.03)

HRT: hormone replacement therapy

c.i.: confidence interval OR: odds ratio

Conclusions

- Breast cancer incidence rapidly returns to pre-screening level in non compliant women
- Post-normal screen breast cancer is a group with adverse prognostic features
- Analysis by time since previous screen shows the influence of both masking effects and force of morbidity