Published in final edited form as:

Breast Cancer Res Treat. 2017 September ; 165(2): 285–291. doi:10.1007/s10549-017-4320-7.

Reassessing risk models for atypical hyperplasia: age may not matter

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Abstract

Purpose—The aim of this study was to investigate the influence of age at diagnosis of atypical hyperplasia (“atypia”, ductal [ADH], lobular [ALH], or severe ADH) on the risk of developing subsequent invasive breast cancer or ductal carcinoma in situ (DCIS).

Methods—Using standard survival analysis methods, we retrospectively analyzed 1353 women not treated with chemoprevention among a cohort of 2370 women diagnosed with atypical hyperplasia to determine the risk relationship between age at diagnosis and subsequent breast cancer.

Results—For all atypia diagnoses combined, our cohort showed a 5-, 10-, and 15-year risk of invasive breast cancer or DCIS of 0.56, 1.25, and 1.30, respectively, with no significant difference in the (65,75] year age group. For women aged (35,75] years, we observed no significant difference in the 15-year risk of invasive breast cancer or DCIS after atypical hyperplasia, although the baseline risk for a 40-year-old woman is approximately 1/8 the risk of a 70-year-old woman. The risks associated with invasive breast cancer or DCIS for women in our cohort diagnosed with ADH, severe ADH, or ALH, regardless of age, were 7.6% (95% CI 5.9–9.3%) at 5 years, 25.1% (20.7–29.2%) at 10 years, and 40.1% (32.8–46.6%) at 15 years.

Conflict of interest Author Giovanni Parmigiani is a member of the Scientific Advisory Board for CRA Health; author Judy E. Garber has research funded by Myriad Genetics, leads a clinical trial for Astra-Zeneca, has a research collaboration with Ambry, and is a consultant for GTx Pharmaceuticals and Helix. All the other authors declare no conflict of interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent: this is a data-analysis only study; this study was approved by the IRB and the informed consent process was waived as there was no direct contact with patients.

Electronic supplementary material The online version of this article (doi:10.1007/s10549-017-4320-7) contains supplementary material, which is available to authorized users.

Conclusion—In contrast to current risk prediction models (e.g., Gail, Tyrer-Cuzick) which assume that the risk of developing breast cancer increases in relation to age at diagnosis of atypia, we found the 15-year cancer risk in our cohort was not significantly different for women between the ages of 35 (excluded) and 75. This implies that the “hits” received by the breast tissue along the “high-risk pathway” to cancer might possibly supersede other factors such as age.

Keywords

Breast atypical hyperplasia; Age; Risk of breast cancer

Introduction

Being diagnosed with atypical ductal hyperplasia (ADH), severe ADH (also known as borderline ductal carcinoma in situ [DCIS]), or atypical lobular hyperplasia (ALH) markedly increases a woman’s risk of developing breast cancer [1–4]. An individual’s predicted risk of breast cancer has significant implications for their clinical management, as a higher risk increases the likelihood that chemoprevention or intensive screening will be recommended.

While it has been suggested that the risk of developing cancer differs depending on the type of atypical hyperplasia (ADH or ALH) [5–7], this has not yet been corroborated by large, recent series. The estimated 10-year risk of invasive breast cancer or DCIS in our cohort of ~1600 women who did not receive chemoprevention was 17.3% after ADH, 20.7% after ALH, and 26.0% after severe ADH [8]. In the Mayo Benign Breast Disease Cohort study, Degnim et al. [3] found that histologic type did not significantly impact breast cancer risk. Both the Gail and the Tyrer-Cuzick (TC) models [10, 11] provide the same risk prediction for women with ADH or ALH and do not have separate calculations for severe ADH. It has also been assumed that the risk of cancer increases with older age at diagnosis of atypia, similar to the general population [9]. Both the Gail and TC models assume that older individuals with atypical hyperplasia will have higher short-term risk. In contrast, Degnim et al. [3] found that younger age at diagnosis was a significant predictor of higher subsequent cancer risk. The goal of our study was to examine the impact of age on the risk of either invasive breast cancer or DCIS in women with atypical hyperplasia.

Methods

As previously described [8], all electronically available breast pathology reports from 1987 to 2010 from three institutions (Massachusetts General Hospital, Brigham and Women’s Hospital, and Newton-Wellesley Hospital) within the Partners Healthcare System, Inc., Boston, MA, were identified under IRB approval. Informed consent process was waived, as there was no direct contact with patients. Using a combined approach of natural language processing and manual verification, all patients with a diagnosis of atypical hyperplasia were identified. Women diagnosed with ADH, ALH, and severe ADH, and with no prior or concurrent (within 6 months) breast cancer, were included as long as they had not undergone bilateral prophylactic mastectomy or taken chemoprevention. While we also studied lobular carcinoma in situ (LCIS), the numbers were too small to be used independently in this analysis. Hence, we limited our analysis to atypical hyperplasias.

If a pathology report contained more than one type of atypical hyperplasia, we assigned what we considered to be the highest risk lesion, deeming severe ADH to be higher risk than ALH, which in turn had a higher risk than ADH. There was no centralized pathology review. If a patient had multiple breast procedures within a 6-month time period, a trumping order was used to assign a maximum diagnosis for that 6-month “episode of care.” Only the patient’s initial highest risk lesion diagnosis was utilized for this study.

Successive breast pathology reports were reviewed to identify women who developed invasive cancer or DCIS. Patient demographics, including age at atypical hyperplasia diagnosis and date of last patient encounter, were obtained from the electronic medical record. The use of chemoprevention was assessed by manual chart review of patient notes and medication lists [8]; because many patients are prescribed chemoprevention and then decide not to take it, follow-up documentation citing that the patient was taking the prescribed medication was required. For the purpose of this paper, we only considered patients who had not been treated with any chemoprevention; in cases where there was no clear documentation about whether the patient taking chemoprevention or not, a “missing” chemoprevention status was recorded, and they were excluded from this analysis. Length of follow-up was defined as the time interval from the date of atypical hyperplasia diagnosis to the date of last patient encounter or date of death.

Our risk analysis was performed using Kaplan–Meier estimators. The logrank test was then used to evaluate possible differences among the survival curves. Age at diagnosis of atypical hyperplasia in our dataset was arbitrarily divided into six 10-year ranges (from (25,35] to (75,85]) and each group contained at least one patient experiencing a subsequent cancer event. Since very few patients were diagnosed with atypical hyperplasia in the extremes of ages of the whole dataset spectrum, ([19,25] and (85,93]), and no patients in either group experienced cancer events following their atypical hyperplasia diagnosis, we excluded them from analysis. Two sensitivity analyses were also performed on 20-year age intervals ((25,45], (55,65], (65,85]), and on the two groups (25,50], (50,85], ideally representing pre-menopausal and post-menopausal women. The results are reported in the supplementary figures S1, S2, and S3.

LCIS diagnoses were included in our original dataset, but we found that the only age group containing a sufficient number of diagnoses of either subsequent invasive breast cancer or DCIS to ensure a reliable estimation of risk was (45,55]. All the other age groups contained either too few cases (<7) or did not provide any observation at a specified time-points (e.g., 15 years), leading to very unstable risk estimations (also confirmed by the wide confidence intervals). For this reason, although we observed a qualitative age pattern similar to the one shown for the other atypia types, we decided to exclude patients with LCIS from this analysis.

A principle of our evaluation was the comparison between our empirical risk estimates and the estimated Gail and TC risks. The Gail model evaluates the absolute risk of invasive breast cancer (but not DCIS) after atypical hyperplasia by integrating information on the relative risk (RR) of breast cancer contributed by one biopsy with the RR contributed by atypical hyperplasia (since atypical hyperplasia cannot be diagnosed without a biopsy).

Settings for the Gail model specify a RR of 3.090 for women aged less than 50, and 2.317 for women over age 50. The following table provides the values of the 10-year risk of breast cancer for a woman in the general population compared to a woman with atypical hyperplasia and no other risk factors when evaluated by TC using the online risk assessment tool available at <http://ibis.ikonopedia.com>:

10-year risk	Age 35	Age 45	Age 55	Age 65	Age 75
Woman with atypia and no other risk factors	4.0%	9.1%	13.0%	15.5%	18.3%
Woman in the general population	1.0%	2.3%	3.2%	3.6%	4.0%
Relative risk (RR)	4.000	3.956	4.062	4.305	4.575

We then estimated the 10-year RR of breast cancer simply by dividing the risk obtained for the individual with atypia by the risk in the general population; the values were mostly consistent with the theoretical risk multiplier of 4.0 introduced in [11].

All statistical analyses were performed using the statistical software R [14], with the “survival” package [15]. To be consistent with the software output, we have indicated age groups using intervals that are open to the left (indicated by a parenthesis) and closed to the right (indicated by a bracket); as an example, the interval (25,35] represented ages from 25 years excluded, to 35 years included.

Results

As shown in the consort plot in Fig. 1, a total of 76,333 breast pathology reports were reviewed from 42,950 unique individuals accrued between 1987 and 2010.

Of these, 2938 women were diagnosed with atypical breast lesions without prior or concurrent cancer, 2370 of which remained after excluding those diagnosed with LCIS and were therefore eligible for this study; among these: 1198 (40.8%) had ADH, 827 (28.1%) had ALH, and 345 (11.7%) had severe ADH. In this same group of patients, no patients aged under () 25 (out of a total of 5), and no patients aged over (>) 85 (out of a total of 4) were diagnosed with breast cancer following their diagnosis of atypia: after excluding these patients, the overall dataset size was reduced to 2361 patients. The mean age at atypia diagnosis in this final group was 53.0 (range 27–85). Overall 1353 (57.3%) individuals in this cohort were known not to have been treated with chemoprevention: of these, 709 (52.4%) had ADH, 483 (35.7%) had ALH, and 161 (11.9%) had severe ADH. The mean age at diagnosis of atypical hyperplasia in this untreated cohort was 52.5 years of age (range 27–84).

Mean follow-up in this untreated cohort was 5.54 years (range 0–23, median 4.58). Specifically, 695 (51.4%) women had between 0 and 5 years of follow-up, 433 (32.0%) had between 5 and 10 years, 133 (9.8%) had between 10 and 15 years, 57 (4.2%) had between 15 and 20 years, and 8 (0.06%) had between 20 and 25 years. Follow-up information was not available for 27 patients (1.9%). Cancer was observed in 74/709 (10.4%) of patients with ADH, in 71/483 (14.7%) of patients with ALH, and in 25/161 (15.5%) of patients with

severe ADH. In these women not treated with chemoprevention, 31 (2.7%) deaths have been observed among those not diagnosed with subsequent breast cancer, and only 5 (3.0%) among those diagnosed with subsequent breast cancer. While not the purpose of this study, this indicates that cancers diagnosed after atypical hyperplasia often have a favorable prognosis.

Analysis of all atypical hyperplasia diagnoses combined

We began our analysis by examining 5-, 10-, and 15-year risk of breast cancer (invasive cancer and DCIS) following a diagnosis of atypical hyperplasia for all atypical hyperplasia diagnoses combined, according to the six age groups (e.g., (25,35], (35,45], etc.). In this scenario, we were not able to detect any significant differences in cancer risk among the various age groups (logrank test p -value at 5 years: 0.598, at 10 years: 0.516, at 15 years: 0.452). As shown in Table 1, for example, for ages (35,45], we observed a 5-year risk of 8.5% (95% CI 4.4–12.4%), whereas for ages (65,75] we observed a 5-year risk of 4.8% (95% CI 1.0–8.5%).

For the same age groups, respectively, the 10- and 15-year risks were equal to 20.1 and 33.7% (95% CI 11.2–28.1%, [19.2–45.7%]) and 25.2 and 43.9% (95% CI 13.4–35.4%, [13.0–63.8%]). We observed that for the age groups (25, 35] and (75, 85], the increased width of the confidence intervals was mainly due to the very small number of cancer events observed (equal to 1 and 5 at 5 years, 1 and 6 at 10 years, and 1 and 6 at 15 years, respectively) following a diagnosis of atypical hyperplasia (Fig. 2).

Analysis of ALH and ADH alone and combined, but excluding severe ADH

When we excluded cases of severe ADH (which was not included in any of the existing risk models), and analyzed the combined ALH and ADH cases only, we were not able to detect a significant difference among the age groups in terms of risk of subsequent breast cancer (logrank test p -value at 5 years: 0.919, at 10 years: 0.695, at 15 years: 0.629) (Table 2).

With either a diagnosis of ALH or ADH in age group (35, 45], we observed an 8.2% risk at 5 years (95% confidence interval 3.9–12.4%), 20.0% risk at 10 years (10.4–28.6%), and 35.4% risk at 15 years (19.3–48.4% at 15 years), whereas for the age group (65,75] we observed a 4.7% risk at 5 years (0.6–8.6%), 20.7% risk at 10 years (9.0–30.9%), and 33.9% risk at 15 years (3.0–54.9%) (Fig. 3).

The 5-year risk for women in age class (65, 75] was 0.57 times the risk of women in age class (35, 45], whereas the risk was almost the same (ratio 1.035) for both these age groups at 10 years. At 25 years, our cohort only reports 27 cases of cancer for patients diagnosed with either ALH or ADH aged (35,45], implying a cumulative risk of 35.4%.

Comparison to predicted risks using gail and TC models

The predicted risk by age group using the Gail and TC models is as follows: using only the relative risks as defined by Gail and TC for one biopsy showing atypia (assuming no other major risk factors), TC version 7 calculates the risk of developing breast cancer (invasive or

DCIS) at 10 years for a woman with atypical hyperplasia at 6.5% if she is 40 years old, but at 15.9% if she is 70. In this case, risk of invasive breast cancer or DCIS at age 70 is calculated as being 2.45 times that at age 40. For similar women, Gail calculates the 5-year risk of breast cancer (invasive only) at 1.7% if she is 40 years old, but at 4.0% if she is 70. In this scenario, the risk of cancer at age 70 is 2.35 times that at age 40.

In an earlier publication [8], we found that a diagnosis of ADH led to significantly fewer predicted breast cancers at 5 years (p -value: 0.036) compared to other forms of atypical hyperplasia. However, our current analysis did not seem to support a significant difference among the age groups within (35,75] with longer follow-up (p -value at 5 years: 0.058, at 10 years: 0.069, overall: 0.092).

There was a clear trend with ADH of no cancers by year 5 if diagnosed before age 35, and for individuals aged 75 or over to experience an increased risk with respect to the other age groups, but the numbers were small and the data may not be reliable (Fig. 4, left panel).

Analysis of ALH and severe ADH

For ALH and severe ADH it looked like the trend of increasing risk with increasing age was completely eliminated (p -value at 5, 10 years and overall, respectively 0.864, 0.937 and 0.843) so we concluded that age was very likely not a factor in breast cancer risk for any age range.

Analysis of all subtypes combined

When all women diagnosed with any type of atypia at any age were combined, the overall 5-year risk of acquiring either invasive breast cancer or DCIS was 7.6% (95% CI 5.9–9.3%), the 10-year risk was 25.1% (20.7–29.2%), and the 15-year risk was 40.1% (32.8–46.6%).

Conclusion

The absolute risk of developing breast cancer up to 15 years following a diagnosis of atypical hyperplasia is widely believed to increase with increasing age [9]. Indeed, this assumption is incorporated into the two major risk assessment models, namely Tyrer-Cuzick and Gail. Tyrer-Cuzick, version 7, reports a 2.45-fold increase in 5-year risk for women age 70 diagnosed with atypical hyperplasia (i.e., a combination of ADH and ALH) with respect to women age 40. The Gail model reports a similar 2.35-fold increase. Our data seem to suggest otherwise. When considering all atypical hyperplasia diagnoses combined, the 5-, 10-, and 15-year risks for invasive breast cancer or DCIS for age group (65,75] were only 0.56, 1.25, and 1.30 times the respective risks for age group (35,45].

From our data, at least for women between age 35 (excluded) and 75, it appears that the breast cancer risk up to 15 years is essentially the same regardless of age at diagnosis of atypical hyperplasia. This is a most interesting finding, since the baseline risk of a normal 70-year-old woman for developing breast cancer (8.9%) is approximately 8 times the baseline risk of a 40-year-old woman (1.1%) [9]. It may seem counterintuitive that this difference is no longer present after the onset of atypical hyperplasia. In addition, if the

absolute risk remains the same regardless of age, then the RR must decrease with age. This finding may be explained by the concept that atypical hyperplasia is a histologic marker that occurs when the breast tissue has accumulated enough “hits” on a “high-risk pathway” to cancer development that supersedes other factors such as age. As such, it is reasonable to state that any woman over age 35 and younger than 75 diagnosed with ADH, severe ADH, or ALH, regardless of their age group, has an equivalent risk of developing either invasive breast cancer or DCIS of 7.6% (95% CI 5.9–9.3%) at 5 years, 25.1% (20.7–29.2%) at 10 years, and 40.1% at 15 years. This may also be true at the extremes of age, but we lack sufficient numbers to be sure.

Prior studies have attempted to determine whether atypical hyperplasia is a true precursor lesion to cancer or if it is a risk indicator. When Hartmann et al. [12] looked at the natural history of atypical hyperplasias, they found features of both. Their study determined that the risk of breast cancer after a diagnosis of ADH or ALH was highest in the first 5 years, consistent with a precursor pathology. However, the risk remained elevated in both breasts long-term, reaching a risk of 29% at 25 years, suggesting that it is also a histologic manifestation of increased risk. Their cohort included patients treated from 1967 to 2001, whereas our study included patients from 1985 to 2010. We believe that the higher estimated breast cancer risks in our current study are likely related to more complete follow-up, increased awareness, and improved screening, particularly in the past decade.

Our data suggest that the 5-to-15 year risk of either invasive breast cancer or DCIS after atypical hyperplasia is the same regardless of age. The short-term risk has implications for the use of chemoprevention, which should be considered if a patient’s 5-year risk is over 1.7% [13]. Based on our study, the 5-year risk exceeds 1.7% for all age ranges.

Even though our study included 1353 patients with atypical hyperplasia, we recognize that it is still a retrospective study with inherent limitations. The small number of cancer events in our dataset results in a lack of power for the analysis (for instance reflected in considerably overlapping confidence intervals). While we show no difference in breast cancer rates based on age, we acknowledge that further studies with more patients, more cancer events, and longer follow-up will be needed to confirm. Unfortunately, we also lack information about family history and other risk factors which could contribute to cancer risk.

While we cannot definitively affirm that breast cancer risks are the same regardless of age at diagnosis of atypical hyperplasia, we believe we have shown a qualitatively interesting tendency, worthwhile of a further validation in a larger dataset. We believe in summary that the risk difference by age is likely to be small, and nowhere near as great as the currently available risk models assume. With that in mind, it may be prudent to use the predicted risks of cancer presented here, regardless of the age of the patient, when counseling patients with atypical hyperplasia rather than relying on current risk models.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

The authors wish to acknowledge Ann S. Adams for writing and editorial assistance.

References

1. Dupont WD, Page DL (1985) Risk factors for breast cancer in women with proliferative breast disease. *N Engl J Med* 312(3):146–151 [PubMed: 3965932]
2. Hartmann LC, Sellers TA, Frost MH et al. (2007) Benign breast disease and the risk of breast cancer. *N Engl J Med* 353(3):229–237
3. Degnim AC, Visscher DW, Berman HK et al. (2007) Stratification of breast cancer risk in women with atypia: a Mayo Cohort Study. *J Clin Oncol* 25(19):2671–2677 [PubMed: 17563394]
4. Choi DX, Eaton AA, Olcese C et al. (2013) Blurry boundaries: do epithelial borderline lesions of the breast and ductal carcinoma in situ have similar rates of subsequent invasive cancer? *Ann Surg Oncol* 20:1302–1310 [PubMed: 23161115]
5. Collins LC, Baer HJ, Tamimi RM et al. (2007) Magnitude and laterality of breast cancer risk according to histologic type of atypical hyperplasia. Results from the Nurses' Health Study. *Cancer* 109(2):180–187 [PubMed: 17154175]
6. Marshall LM, Hunter DJ, Connolly JL et al. (1997) Risk of breast cancer associated with atypical hyperplasia of lobular and ductal types. *Cancer Epidemiol Biomark Prev* 6:297–301
7. Zhou WB, Xue DQ, Liu XA et al. (2011) The influence of family history and histological stratification on breast cancer risk in women with benign breast disease: a meta-analysis. *J Cancer Res Clin Oncol* 137(7):1053–1060 [PubMed: 21499874]
8. Coopey SB, Mazzola E, Buckley JM et al. (2012) The role of chemoprevention in modifying the risk of breast cancer in women with atypical breast lesions. *Breast Cancer Res Treat* 136:627–633 [PubMed: 23117858]
9. Feuer EJ, Wun LM, Boring CC et al. (1993) The lifetime risk of developing breast cancer. *J Natl Cancer Inst* 85(11):892–897 [PubMed: 8492317]
10. Gail MH, Brinton LA, Byar DP et al. (1989) Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst* 81:1879–1886 [PubMed: 2593165]
11. Tyrer J, Duffy SW, Cuzick J (2004) A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med* 23:1111–1130 [PubMed: 15057881]
12. Hartmann LC, Radisky DC, Frost MH et al. (2014) Understanding the premalignant potential of atypical hyperplasia through its natural history: a longitudinal cohort study. *Cancer Prev Res* 7:211–217
13. Visvanathan K, Hurley P, Bantug E et al. (2013) Use of pharmacologic interventions for breast cancer risk reduction: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 31:1–22 [PubMed: 23129739]
14. Ihaka R, Gentleman R (1996) A language for data analysis and graphics. *J Comput Graph Stat* 5(3):299–314
15. Therneau T (2015) A package for survival analysis in S. Version 2.38, <http://CRAN.R-project.org/package=survival>

Fig. 1.
Consort plot describing the structure of the studied cohort and the exclusions from the original dataset

Fig. 2.
Kaplan–Meier estimates for the 15-year risk of either invasive breast cancer or DCIS following a diagnosis of atypical hyperplasia, for all atypical hyperplasia types combined

Fig. 3.
Kaplan–Meier estimates for the 15-year risk of either invasive breast cancer or DCIS following a diagnosis of atypical hyperplasia, for ADH and ALH combined

Fig. 4.
Kaplan–Meier estimates for the 15-year risk of either invasive breast cancer or DCIS
following a diagnosis of ADH (*left panel*) and ALH and severe ADH combined (*right panel*)

Table 1

5-, 10-, and 15-year risk of invasive breast cancer following a diagnosis of atypical hyperplasia, for all atypical hyperplasia diagnoses combined, with corresponding 95% confidence intervals, and *p*-values of the overall logrank test

Age group	5-year risk (%)	95% CI	10-year risk (%)	95% CI	15-year risk (%)	95% CI
(25,35]	4.0	(0.0, 11.4)	4.0	(0.0, 11.4)	4.0	(0.0, 11.4)
(35,45]	8.5	(4.4, 12.4)	20.1	(11.2, 28.1)	33.7	(19.2, 45.7)
(45,55]	7.8	(5.1, 10.4)	25.6	(18.6, 31.9)	43.8	(31.3, 53.9)
(55,65]	7.2	(3.6, 10.7)	30.4	(19.6, 39.7)	40.3	(24.7, 52.7)
(65,75]	4.8	(1.0, 8.5)	25.2	(13.4, 35.4)	43.9	(13.0, 63.8)
(75,85]	15.3	(1.8, 26.9)	20.9	(3.4, 35.2)	20.9	(3.4, 35.2)
<i>p</i> -value	0.598	-	0.516	-	0.452	-

Table 2

5-, 10-, and 15-year risk of either invasive breast cancer or DCIS, with corresponding 95%-confidence intervals and *p* values of the overall logrank test, following a diagnosis of atypical hyperplasia, for ADH and ALH

Age group	5-year risk (%)	95% CI	10-year risk (%)	95% CI	15-year risk (%)	95% CI
(25,35]	4.8	(0.0, 13.4)	4.8	(0.0, 13.4)	4.8	(0.0, 13.4)
(35,45]	8.2	(3.9, 12.4)	20.0	(10.4, 28.6)	35.4	(19.3, 48.4)
(45,55]	8.2	(5.2, 11.1)	24.7	(17.4, 31.4)	44.7	(31.3, 55.5)
(55,65]	7.0	(3.2, 10.7)	29.1	(18.1, 38.7)	39.2	(23.3, 51.9)
(65,75]	4.7	(0.6, 8.6)	20.7	(9.0, 30.9)	33.9	(3.0, 54.9)
(75,85]	10.8	(0.0, 21.7)	16.7	(0.0, 31.0)	16.7	(0.0, 31.0)
<i>p</i> -value	0.919	-	0.695	-	0.629	-