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Short report

Similar prevalence of founder *BRCA1* and *BRCA2* mutations among Ashkenazi and non-Ashkenazi men with breast cancer: Evidence from 261 cases in Israel, 1976–1999

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Abstract

To evaluate the potential contribution of mutations in the *BRCA1* and *BRCA2* genes to male breast cancer (MBC), we expanded a previous study to screen a total of 261 Israeli men diagnosed with breast carcinoma. A total of 21 *BRCA2 6174delT* and 8 *BRCA1 185delAG* mutations were found. Similar frequencies of *BRCA1* and *BRCA2* mutation carriers were found among Ashkenazi (12.8%) and non-Ashkenazi Jews (9.1%). The combined prevalence of *BRCA1/BRCA2* founder mutations among Ashkenazi Jewish men is slightly higher than for women, due to a higher frequency of *BRCA2* mutations.

Keywords: *BRCA1* mutation; *BRCA2* mutation; Male breast cancer; Epidemiology; Israel

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1. Introduction

With approximately 1700 new cases expected to occur in 2006, male breast cancer (MBC) accounts for only 0.7% of all breast cancer diagnosed in the US [1]. However, the disease incidence in the US is increasing and has climbed 26% over the past 25 years [2]. Similarly, the annual age-standardized incidence rate in Israeli Ashkenazi Jews (persons whose families immigrated to Israel from Europe or America) has been steadily increasing from 9 in 1980 to 12 per million in 1997 [3]. In contrast, the annual rates among non-Ashkenazi Jews (people from families originating from Mediterranean regions), who comprise approximately 45% of the 1 million Jewish men over 40 years of age living in Israel [4], remained around 7 per million over the same time period. Breast carcinoma has also been observed to be more common among American Jewish men, a population of predominantly Ashkenazi origin, compared to other non-Jewish Americans [5–8].

The functionally defective mutations of *BRCA1* and *BRCA2* are associated with increased breast cancer risk; however, such mutations are relatively rare in unselected cancer patients. The frequency of three founder germline mutations in the tumor suppressor genes *BRCA1* and *BRCA2* among unselected Ashkenazi women with breast cancer is roughly 10%, and is much higher in multiple-case families [9–11]. These observations led us to conduct an earlier population-based study on these founder mutations of MBC patients in Israel. We found that 15% of the 89 Ashkenazi patients examined were carriers of the *BRCA2 6174delT* mutation [12]. Surprisingly, we also found two carriers of this mutation among 21 non-Ashkenazi MBC Jewish patients. This was the first published observation of this mutation among non-Ashkenazi Jews suggesting a common ancestor *BRCA2 6174delT* emerged prior to the divergence of these groups, similar to *BRCA1 185delAG* mutation [13]. Since our publication, two other studies of Ashkenazi men [14,15] have been published, but they had a relatively small number of cases ($n < 30$). We therefore expanded our study by including patients from additional hospitals to better estimate the frequency of *BRCA1* and *BRCA2* mutations among Israeli MBC patients.

2. Patients and methods

The current study includes all 269 MBC cases who were diagnosed in 16 hospitals throughout Israel between 1976 and 1999, including the 110 subjects in our first report [12]. The cases available for the study represent half of the total number of incident MBCs in the country during this period [16]. Eight subjects did not have adequate pathological material for mutation status and marker genotypes, leaving 261 in the study sample. The laboratory methods for the three founder mutations *185delAG* and *5382insC* in *BRCA1* and *6174delT* in *BRCA2* were as previously described [12].

Jewish patients were characterized either as Ashkenazi or non-Ashkenazi, based on the recorded place of birth in the Israeli Population Registry or, if they were born in Israel, their fathers' recorded place of birth. Patients who were born in the former USSR ($n = 52$), other Eastern European countries ($n = 79$), Central or Western Europe ($n = 29$), America ($n = 4$), South Africa ($n = 1$), or who were born to fathers from these areas ($n = 23$) were categorized as Ashkenazi Jews. Non-Ashkenazi Jews were either born in North Africa ($n = 27$), the Middle East ($n = 15$), Bulgaria ($n = 3$), Greece ($n = 2$), Ethiopia ($n = 2$), Afghanistan ($n = 2$), or their fathers were from those areas ($n = 4$). Non-Jewish Israeli-born were designated as Arabs ($n = 16$). Two patients born in Israel, who were sons of Israeli-born fathers, were categorized