

Quality of Life in Asymptomatic BRCA1/2 Mutation Carriers

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Quality of Life

QOL is a personal and multidimensional concept.

Physical, functional, psychological, social and spiritual aspects are fundamental domains of QOL.

Health related QOL

To date, most studies investigating measures of HR-QOL have been conducted on cancer patients and survivors.

HR-QOL is considered to be a significant medical outcome with high prognostic value in chronic illnesses.

In patients with breast cancer, poor HR-QOL shortly after diagnosis and during treatment was mediated by fatigue (Meeske et al.2007).

HR-QOL in asymptomatic BRCA1/2 mutation carriers

The few studies investigating QOL among asymptomatic high-risk women have been conducted within the context of women who had undergone prophylactic oophorectomy or surveillance.

Overall, women opting for surveillance compared to prophylactic oophorectomy had lower scores on measures of QOL.

Psychological measures in asymptomatic BRCA1/2 mutation carriers

Despite the assumption that oncogenetic diagnosis may incur psychological distress, major symptoms have not been found consequent to genetic testing.

Still, few studies have identified patients most prone to distress - these include probands and those who received inconclusive results.



Hypothesis

Despite the lack of evidence of negative psychological outcomes in carriers, it is plausible to assume that being at high risk may result in subtle disturbances that may lead to symptoms associated with impaired quality of life.



Objective

To investigate the association between positive genetic diagnosis for BRCA1/2 founder mutations and QOL in Ashkenazi asymptomatic women.

Study model

| Independent variable | Mediated variables | Dependent variables |
|--|---|--|
| <p data-bbox="85 468 537 773">BRCA1/2 carrier status: positive negative low risk control</p> | <p data-bbox="595 468 1309 654">Psychological distress: anxiety, depression, somatization, etc. (BSI)</p> <p data-bbox="595 659 1309 773">Cognitive appraisal: cancer related worry (CRW)</p> <p data-bbox="595 779 1309 1093">Clinical: family history of cancer; age at genetic diagnosis; surveillance protocols; menopausal symptoms</p> <p data-bbox="595 1099 1309 1282">Socio-demographic: family status; have children; education; income</p> | <p data-bbox="1379 468 1843 902">Daily functioning: quality of life (SF-36); fatigue (FSI); quality of sleep (PSQI), actigraph.</p> |



Methods

Case-control retrospective design.

High Risk (n=37)

BRCA1/2 carriers (n=17)

non-carriers (n=20)

Low Risk (n=36)



Measures

All women updated socio-demographic and clinical status during interviews

Participants completed a battery of questionnaires including psychological variables (BSI, CRW), QOL (SF-36), QOS (PSQI) and fatigue (FSI).

Socio-demographic variables

| | Total | High-Risk | | Controls | P value |
|-----------------------------|-----------|--------------------------|------------------------------|-----------|---------|
| | n=73 | BRCA1/2 carriers n=17 | BRCA1/2 non-carriers n=20 | n=36 | |
| Age (mean±SD) | 51.54±8.9 | 51.41±9.11 | 54.50±9.37 | 49.96±8.3 | p=0.188 |
| Age at testing (mean±SD) | 45.03±9.0 | 43.82±8.85 | 46.05±9.14 | - | p=0.459 |
| Follow-up (mean±SD) | 8.05±1.9 | 7.59±2.48 | 8.45±1.10 | - | p=0.198 |
| Family Status (n, %) | | | | | |
| Married | 61 (83.6) | 15 (88.2) | 17 (85.0) | 29 (80.6) | |
| Not-married | 12 (12.4) | 1 (5.9) | 3 (15) | 7 (19.4) | |
| Have Children (n, %) | | | | | |
| Yes | 71 (97.3) | 16 (94.1) | 20 (100) | 35 (97.2) | |
| No | 2 (2.7) | 1 (5.9) | - | 1 (2.8) | p=0.551 |
| Education (n, %) | | | | | |
| High-School | 14 (19.2) | 8 (47.1) | 3 (15.0) | 3 (8.3) | |
| College | 7 (9.6) | 3 (17.6) | 3 (15.0) | 1 (2.8) | |
| Graduate | 52 (71.2) | 6 (35.3) | 14 (70.0) | 32 (88.9) | p=0.002 |
| Income (n, %) | | | | | |
| Lower than average | 3 (4.2) | 1 (5.9) | - | 2 (5.6) | |
| Average | 37 (51.4) | 9 (52.9) | 10 (50) | 18 (50) | |
| Higher than average | 32 (44.4) | 7 (41.2) | 10 (50) | 16 (44.4) | p=0.881 |

Clinical variables

| | Total | High-Risk | | Controls | P value |
|-----------------------------------|-----------|--------------------------|------------------------------|-----------|---------|
| | n=73 | BRCA1/2 carriers n=17 | BRCA1/2 non-carriers n=20 | n=36 | |
| Family History (n, %) | | | | | |
| Breast-ovarian cancer | 34 (46.6) | 17 (100) | 17 (85.0) | - | |
| Other cancer | 14 (19.2) | - | 3 (15.0) | 11 (30.5) | |
| No family history | 25 (34.2) | - | - | 25 (69.5) | p=0.001 |
| PO (n, %) | | | | | |
| Yes | | 14 (82.3) | | | |
| No | | 3 (17.7) | | | |
| Menopausal Symptoms (n, %) | | | | | |
| Yes | 13 (17.8) | 6 (35.3) | 5 (25) | 2 (5.5) | |
| No | 60 (82.2) | 11 (64.7) | 15 (75) | 34 (94.5) | p=0.055 |
| CRW (mean±SD) | 0.58±0.48 | 0.75±0.53 | 0.67±0.48 | 0.45±0.44 | p=0.067 |
| BSI Total (mean±SD) | 0.52±0.42 | 0.53±0.48 | 0.41±0.36 | 0.57±0.42 | p=0.37 |

Quality of Life

| | Total n=73 | High-Risk | | Controls n=36 | P value |
|---|---------------|-----------------------------|---------------------------------|------------------|---------|
| | | BRCA1/2 carriers n=17 | BRCA1/2 non-carriers n=20 | | |
| QOL (mean±SD) | | | | | |
| Physical functioning | 88.63±15.28 | 82.35±19.05 | 87.0±18.81 | 92.50±9.30 | 0.067 |
| Role limitation due to physical problems | 88.70±23.56 | 79.41±30.92 | 85.0±28.56 | 95.14±13.12 | 0.049 |
| Pain | 74.07±21.88 | 71.65±28.54 | 71.65±22.48 | 76.56±18.04 | 0.638 |
| General health | 72.50±18.04 | 69.71±22.14 | 72.93±20.64 | 73.58±14.46 | 0.765 |
| Vitality | 63.47±19.64 | 60.20±25.93 | 67.75±16.18 | 62.64±17.79 | 0.475 |
| Social functioning | 90.42±16.98 | 86.79±19.46 | 89.38±14.78 | 92.71±17.0 | 0.477 |
| Role limitation due to emotional problems | 90.41±23.23 | 74.51±36.38 | 91.67±21.29 | 97.22±9.34 | 0.003 |
| Mental health | 74.78±14.73 | 73.58±17.26 | 77.20±14.04 | 74.0±13.87 | 0.689 |
| Total | 80.29±13.94 | 74.41±19.21 | 80.32±13.74 | 83.04±10.20 | 0.108 |

Summary

Impaired QOL was found in asymptomatic BRCA1/2 mutation carriers compared to non-carriers and controls.

The strongest domain of QOL affected by carrier status was role limitation due to emotional problems.

It is yet to be explained if these findings are mediated by lower levels of education and/or CRW.

Quality of Sleep and Fatigue

| | Total | High-Risk | | Controls | P value |
|--------------------------------|-----------|--------------------------|------------------------------|-----------|---------|
| | n=73 | BRCA1/2 carriers n=17 | BRCA1/2 non-carriers n=20 | n=36 | |
| QOS (mean±SD) | | | | | |
| Sleep latency (minutes) | 16.4±17.5 | 20.8±17.3 | 18.2±25.8 | 13.3±11.3 | 0.305 |
| Sleep efficiency (%) | 91.4±10.0 | 85.3±13.6 | 93.7±8.7 | 93.1±7.2 | 0.030 |
| PSQI Total | 4.8±3.3 | 7.0±4.3 | 3.76±2.4 | 4.2±2.8 | 0.011 |
| Actigraph | | | | | |
| Sleep latency (minutes) | 8.7±9.7 | 12.2±14.36 | 4.75±6.12 | 9.0±7.85 | 0.049 |
| Sleep efficiency (%) | 96.54±5.7 | 94.46±10.6 | 97.13±2.02 | 97.25±2.9 | 0.395 |
| FSI Total | 2.76±17.6 | 6.38±18.9 | -0.94±15.35 | 2.91±18.2 | 0.501 |

Quality of Sleep and Fatigue summary

Compromised quality of sleep were found in BRCA1/2 mutation carriers compared to non-carriers and controls both in self report and objective instrument (actigraph).

Higher levels of fatigue were not found in carriers compared to non-carriers and controls.

סיכום

- נשים שעברו בדיקה גנטית ונמצאו נשאים למוטציה בגנים BRCA1/2 סובלות מפגיעה באיכות השינה, מירידה בתפקוד הקשורה במצב הנפשי ומדאגה ממחלת הסרטן
- נשים אלו אינן שונות מנשים שאינן נשאים ומנשים שלא עברו בדיקה גנטית במאפיינים פסיכולוגיים, ברמת העייפות ובמאפיינים אחרים של בריאות ואיכות חיים
- לא ניתן להסביר את הפגיעה באיכות השינה וברמת התפקוד באמצעות מדדים פסיכולוגיים או דמוגרפיים

מסקנות

- ניתן להצביע על סימנים של פגיעה בתפקוד בקרב נשים נשאות, המתבטאים בעיקר בנדודי שינה ובהשפעת המצב הנפשי על רמת התפקוד
- ניתן להניח כי נדודי שינה מהווים גורם סיכון לפגיעה בתפקוד על רקע נפשי
- הופעת נדודי שינה באוכלוסיה זו קודמת להופעת המחלה עצמה, וייתכן שהגורם הקוגניטיבי של הדאגה מהמחלה מהווה את הסטרסור המניע להופעתם של נדודי שינה

הפרעות שינה בנשים בסיכון לחלות בסרטן השד / שחלה

חשיבות המחקר:

- חשיבות מעשית: איתור סימנים של הפרעות שינה ועייפות לאחר האבחון הגנטי ובמהלך המעקב השוטף על מנת לטפל בבעיות אלו ולשפר איכות חיים ותפקוד יומי
- חשיבות תיאורטית: הבנת מהלך ההתפתחות הטבעי של נדודי שינה בצל סיכון אולם ללא מחלה פעילה ו/או טיפול