The Breast 46 (2019) 48–51

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

# Current knowledge of risk reducing mastectomy: Indications, techniques, results, benefits, harms

Andrew D. Baildam

*Consultant Oncoplastic Breast Surgeon, King Edward VII's Hospital London, UK*

ARTICLE INFO

*Article history:*
Received 20 March 2019
Accepted 28 March 2019
Available online 29 March 2019

ABSTRACT

The last twenty years have seen a complete change in society's attitude to the strategy of risk reduction of breast cancer in high-risk individuals by means of proactive mastectomy. Once termed 'prophylactic mastectomy', risk reducing mastectomy (RRM) was considered two decades ago not only extreme, but in some quarters almost unethical. RRM is now commonly undertaken in specialist breast units for women at high individual breast cancer risk, by virtue of an inherited breast cancer related gene mutation or from calculated high statistical risk from family history data, and the efficacy of RRM in reducing subsequent incident diagnoses of breast cancer has been published from a number of centres. RRM is offered routinely in conjunction with total breast reconstruction, using the whole range of reconstructive surgical techniques.

The public announcement by the actor Angelina Jolie in 2013 that she had inherited and harboured a BRCA1 gene mutation, and was undergoing RRM and breast reconstruction to lower her intrinsic breast cancer risk, had a significant effect on public attitudes and perception. Whilst there are other means of lowering breast cancer risk by means of selective oestrogen receptor modulators, such as tamoxifen and raloxifene, their lowering effect on risk of breast cancer remains substantially less than that afforded by surgical removal of 'at risk' breast tissue. The progressive development and increasing sophistication of techniques of breast reconstructive surgery has paralleled the trend for more RRM surgery, and the substantial majority of women who opt for RRM choose immediate breast reconstruction.



## 1. Indications

The strongest predictor of breast cancer risk in an individual is the presence of a significant family history of breast cancer. Breast cancers occurring at young ages and the presence of multiple breast cancers in any individual family member, are highly suggestive of a breast cancer related gene mutation. Almost 30% of breast cancers in women <30 years at diagnosis are due to the known mutations BRCA1, BRCA2 and TP53 [1,2]. Studies have found that 70–85% of BRCA1 and BRCA2 mutation carriers may develop breast cancer, the risk being slightly lower for BRCA2 carriers [3–6].

The prevalence of breast cancer associated gene mutations depends upon each country and most especially on the ethnic origin of families. For example the Ashkenazy Jewish population has three founding mutations, across BRCA1 and BRCA2. These three mutations are found in over 2% of the Ashkenazy population. One study found that one of the three mutations was present in 59% of high risk families [7]. Once a certain breast cancer related mutation has been found in a family, such as BRCA1 or BRCA2, definitive genetic testing for individuals is possible. Genetic testing over the last several years has become increasingly available, commercially marketed and very much cheaper in terms of financial cost. The most recent tests available commercially are based on buccal swabs from the mouth, or saliva, obviating even a blood test. The analysis of known gene mutations is conducted in an automated basis at low cost, with the results typically available within six weeks.

Any individual found to carry a breast cancer related gene mutation should be offered information, advice and counseling about risk reducing strategies including surgical intervention.

If it has not been possible to demonstrate a breast cancer related gene mutation, risk estimation for a single individual can be calculated. This is based upon large epidemiological studies. An individual may be advised on the basis of risk estimation, but it is important to distinguish between lifetime overall risk and age specific risk. Risk does decrease with age and whilst RRM may be entirely appropriate for young and middle aged woman, as years of

*E-mail address:* ad.baildam@bmichoice.co.uk.

https://doi.org/10.1016/j.breast.2019.03.011
0960-9776/

risk are lived through, the overall risk decreases. Within Europe risk estimation is based mainly on Claus data [8–10]. Within North America the Gail model is widely used [11]. There are a number of specific computer programs now available and increasingly used such as Tyrer-Cusick, BOADICEA and BRCA-Pro [12]. Within the United Kingdom Tyrer-Cusick is now the most widely used program, containing as it does most of the currently known risk factors for breast cancer, including at its most recent update, radiological breast density on mammography [13].

Generally if an indiviudual's lifetime risk is calculated at 25% or more then it is appropriate to offer the process of consultations about RRM. The Manchester group, anticipating the difficulty of the subject of risk assessment, published in 2002 a protocol for the management of women at high risk of breast cancer [14]. Whilst the means of calculating risk and the automation of related gene mutation analysis has transformed over the last several years, the protocol remains a useful tool for advising patients appropriately to the option of surgery.

In a survey of 10 European centres, only three, Manchester, Edinburgh and Heidelberg/Dusseldorf, routinely offered the possibility of RRM to women with a lifetime risk of 25% or greater [15]. Many centres only mention RRM to potential mutation carriers keen to undertake a genetic test. There is a geographical shift across Europe from north to south in attitudes to RRM, with RRM being less common in the southern European countries compared with countries in northern Europe [16–18].

Confirmation of the breast cancers in the family is paramount. Instances of fabricated family history have been reported [19]. There are some fairly clear contraindications to proceed with RRM surgery and these listed in Table 1.

## 2. Techniques

The objective of RRM is to reduce breast cancer risk and breast cancer mortality, but proactive surgery also can reduce psychological distress and anxiety. Clinic consultations should take place in unhurried appointments. Several visits should be offered over a period of months with time for reflection and consideration such that all aspects, including consultation with a psychologist, are covered [20].

There is no objectively defined single technique for RRM and several approaches of surgery can be offered, so long as the proposed surgery optimizes equipoise between reduction effectiveness and functional outcomes. Techniques encompass types of skin-sparing mastectomy and all options of breast reconstruction.

**Table 1**
Contraindications against Risk Reducing Mastectomy.

| |
|---|
| **Absolute contraindications** |
| Failure to confirm high-risk status of individual |
| Proof of non-gene mutation carrier in a proven gene-carrying heritage |
| Falsified family history and Munchausen's syndrome |
| Decision not the individual's own choice |
| Awaiting individual result of a gene mutation testing |
| Refusal to accept complication risks |
| Surgeon inexperience in RRM and breast reconstruction |
| **Relative contraindications** |
| Awaiting further consultations with geneticists/surgeons |
| Decision uncertainty |
| Psychological concerns |
| Family dysfunction, eg sibling disagreement on RRM |
| Psychiatric disorders – clinical depression, schizo-affective disorder, clinical anxiety state |
| Body dysmorphia |
| Unrealistic expectation of outcome – aesthetic as well as prevention |
| Choosing RRM is for 'cosmetic' reasons rather than oncological |

Clearly individual preferences, breast size and shape are all important, as is the experience and wisdom of the surgeon. In the absence of a single described binary operation, most centres have developed techniques over the years based on their own surgeons' aptitudes and training. There must be dedicated breast and reconstructive surgery available, and these skills may be found both in teams as well as in individual surgeons, provided that they have had appropriate and thorough training both in aspects of breast oncology surgery and breast reconstructive surgery.

All surgical procedures require a fully informed discussion of benefits and risks. There is no randomised trial evidence and all RRM data is from cohort studies. Risk reduction from surgery is well over 90% but cannot ever reach 100%. It is important that individual women understand that even after RRM there is a small chance they could be diagnosed at a later date with breast cancer. Even with surgery planned and delivered to the highest level, the patient must be informed fully about body changes which occur and their impact on body image, possible complications from surgery and anaesthesia, and potential revision surgery in the longer term.

The surgical techniques used for RRM are evolving and continue to do so, with aesthetic outcomes generally improving with advances in reconstructive surgery and in materials available. There never was, and has never been a definition of RRM and no formal description of 'the operation'. There is no 'standard' operation, but there should be removal of '*all at risk*' glandular tissue. The main choices centre around the extent of mastectomy - 'conventional' without breast reconstruction and skin sparing techniques with reconstruction, with careful minimisation of scarring. Most operations are judged by outcome, not by how they are technically performed. The operation has been progressively engineered over two decades, with the objective of reducing breast cancer risk substantially as well as producing acceptable functional and quality of life outcomes. The description of development of the range of surgical techniques, incisions used, nipple sparing and nipple preserving, complications from surgery as well as diagrams and photographs of outcomes has been published in detail elsewhere [21]. To this list of surgical approaches now is added that of a circumareolar incision for mastectomy with NAC removal - a 'type 5' skin sparing approach, and the circumareolar donut incision with nipple preservation on a de-epithelialised bridge pedicle, a 'type 6' skin sparing mastectomy. Nipple necrosis after attempted surgical preservation occurs in a small minority of patients. Optimisation of nipple survival is claimed to be most achievable with delayed pedicle incision, with RRM preformed at a second operation after initial NAC pedicle isolation [22].

Early RRM surgeons adopted nipple/areola complex-sparing (NAC) techniques as well as skin-sparing approaches. There are technical challenges to NAC preservation which revolve around maintaining an adequate vascularity, and in a large deeply ptotic breast the requirement for a significant parenchymal pedicle means that NAC preservation can be both problematic as well as unwise, due to the inevitability of residual, potentially 'at risk' breast tissue. But for the less ptotic and smaller breast NAC retention is possible, aesthetically and superior to NAC reconstruction, and is oncologically safe [23–25]. For patients who can choose NAC conservation it is often said that the NAC retention may also carry an added 5% of lifetime breast cancer risk. But the evidence does not support this. Increasingly in patients undergoing mastectomy who have been diagnosed with breast cancer, NAC preservation is safely offered [26]. Preservation of the natural nipple does lead to better psychosocial functioning, and higher levels both of satisfaction and sexual well-being compared to women who have had the NACs surgically removed as part of the mastectomy [27,28].

The whole range of breast reconstructive procedures, including microvascular DIEP flaps, should be available and be offered and

discussed with patients so they are able to make fully informed decisions. The overwhelming majority of women undergoing RRM choose implant based breast reconstruction. This may be with total submuscular insertion of tissue expanders followed after clinic expansion visits, by insertion of permanent implants several months later, or by using acellular dermal matrix (ADM) either over tissue expanders, or more commonly, with immediate permanent implants. ADM is inserted as an internal 'bra cup', sutured over the implant, to the edge of a mobilized pectoralis major superiorly and to the internal inframammary fold inferiorly. More recently complete ADM templates, commercially available, are used to enclose and support the implants without the need to disturb the anterior chest wall musculature in any way. Results on outcomes with these newer techniques are awaited.

The use of a single operation to achieve RRM with immediate implant reconstruction is efficient in time, surgical expertise, patient recovery and cost, but requires the use of porcine or bovine derived ADM. But many women do not accept an ADM implanted surgically, and there are no long-term data on its outcomes as yet. For these women we have innovated a technique which does require two operations, but avoids both the discomfort and repeat clinic visits of tissue expansion and the use of an ADM. The first operation involves placement of bilateral permanent implants in a dual plane position behind the pectoralis major superiorly and the breast parenchyma inferiorly. Several months later the RRM operation is performed leaving the permanent implants intact and undisturbed, beneath the pectoralis major and the sheet of capsular pocket which the healing process has laid down inferiorly over the breast implant. Essentially through the healing process around the implant the body creates its own sheet of ADM [29].

## 3. Results

### 3.1. Benefits and harms

RRM as a concept was in the late 1990s vigorously opposed by some, and in some quarters the surgeons tentatively undertaking RRM were heavily criticized [30]. The patients selected themselves, usually pushed for this then-unproven intervention, and they as much as the surgeons were pioneers. Presumably unfamiliar with advances in breast aesthetic surgery and breast reconstruction, an Editorial comment in the British Medical Journal stated 'these patients must choose between mutilation and death, and this is barbarism, pure and simple' [31]. It was some years before data on outcomes were becoming available.

There are no randomised controlled studies on RRM. The best evidence for the lowering effect on the subsequent diagnosis of breast cancer comes from cohort studies. Among the first of these was the experience of the Mayo Clinic where for some time bilateral mastectomy for profuse benign proliferative disease had been practiced. In women at high risk for breast cancer by virtue of family history, RRM lowered the subsequent incidence of breast cancer diagnosis by >90% [32,33]. The subsequent breast cancer risk is emphatically lowered in proven BRCA1 and BRCA2 gene carriers [34,35]. This risk-lowering effect has been seen in all the studies published so far. The reduction of breast cancer incidence in BRCA1 and BRCA2 mutation carriers was equally large in the Dutch and other series [36,37]. Whilst the risk-reducing effect is seen similarly across nations, uptake of RRM and its cultural acceptability differ, with uptake far higher in north European countries compared to the southern neighbours [38,39].

The reduction of risk of subsequent breast cancer diagnosis is proven after RRM, but in many quarters the undertaking of the surgery is still controversial. It has been suggested that the remaining risk is proportional to the volume of breast tissue not excised at RRM – it is technically impossible to remove surgically every last piece of breast parenchyma – but there is no evidence to support what appears to be a simple presumption. In practice the situation is almost certainly far more complex. There will never be a randomised trial on the efficacy of RRM, and cohort studies have given sufficient information regarding breast cancer risk reduction.

The majority of women who undergo RRM choose to have breast reconstruction at the same time, and the majority of these choose an expander/implant-based process. Whether the woman can be offered nipple areolar complex (NAC) preservation technically depends upon the size and ptosis of the breast. But to preserve successfully the viable vascularized NAC in a large ptotic breast requires a significant preservation pedicle, and this may contain viable breast parenchyma with remaining cancer potential. But for women with more moderate breast size and less ptosis shape NAC conservation seems not to increase remaining risk [40]. Women who are able to have their NAC preserved are more likely to have better body image and sexual wholeness then those in whom the NACs are removed, even with subsequent NAC reconstruction [41].

It would be unlikely that studies would universally give positive outcomes for RRM, and there are reports of negative effects on body image after RRM - but these have not distinguished between the different types of breast reconstruction offered, or in one study, RRM with no reconstruction [42–44]. These studies add to the published data on distress associated with knowledge of bearing a high-risk gene, or a calculated high risk status [45,46], and having to make choices as a consequence of that information [47]. Graves and Metcalfe also found that women who chose to have RRM instead of surveillance alone did demonstrate a decline in cancer-related distress within two years after a positive BRCA test. This demonstrates that interventional surgery does confer psychological benefit as well as risk reduction. What a published study cannot do is to highlight the comments that individual women may make having chosen surgery. Commonly these express profound relief that something has been achieved and the risk has been substantially lowered. It is not unusual on follow-up for a woman to state that she has become the oldest living female family member in several generations, after one of two decades after having RRM, remaining cancer-free.

There are some women who undergo RRM on the basis of risk calculation, but in whose family no specific breast cancer related gene has been found at the time of surgery. In the years after RRM, a cancer related gene may be found, and the woman may test negative for carrier status. Anecdotally this small number also express profound relief that they now know they cannot transfer that gene to their children - as they do not carry it. The surgeon may hear that they made the decision for surgery based upon the best knowledge at the time, and do neither resent nor regret the decision. Their own breast cancer risk is therefore minute.

All breast reconstructive surgery carries risks and limitations, and scarring. Even with flawless recovery there will be a high chance of further surgical intervention at some point in a woman's journey. Implants do need to be changed, at the present time probably every 12–15 years. This is lengthening as implant technology progresses, and does involve surgery and expense, and recovery. Such operations are minor compared to the initial RRM. Women with autologous tissue flaps, LD back flaps and DIEP flaps, always have the scarring and possible sensory disturbance at the donor site, and this can be troubling. Women must be advised that this is going to be a lifelong commitment. Although fundamentally different, some may think of RRM as a kind of 'cosmetic surgery', but women who do have aesthetic surgery for otherwise intact and normal breasts do themselves after surgery have the same long-term issues, though this may be seldom have been discussed beforehand.

Nevertheless all studies published to date demonstrate a subsequent substantial decline in the diagnosis of breast cancer in the years following RRM surgery, and this diminution is maintained over time. The lessening of cancer incidence in high-risk women is >90%, and this holds true whether or not the nipple areolar complex is preserved or reconstructed. The overwhelming majority of women have immediate breast reconstruction, and these techniques may need some sort of longer-term surgical maintenance. There are potential psychosocial sequelae, and effect on body image, and women need to be aware ahead of surgery of these issues. But the lowering of breast cancer risk is of the highest therapeutic outcome in all data so far. There never will be randomised trials of RRM, the challenge now is to find less invasive techniques and interventions that will have the same significant risk-lowering effect without the tribulations of surgery.

## References


[1] Claus EB, Risch N. Thompson WD Autosomal dominant inheritance for early-onset breast cancer Implications for risk prediction. Cancer 1994;73(3):643–51.
[2] Evans DG, Moran A, Hartley R, et al. Long term outcomes of breast cancer in women aged 30 years or younger, based on family history, pathology and BRCA1/BRCA2/TP53 status. Br J Canc 2010;102(7):1091–8.
[3] Ford D, Easton DF, Stratton M, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. Am J Hum Genet 1998;62(3):676–89.
[4] Ford D, Easton DF, Bishop DT, et al. Risks of cancer in BRCA1-mutation carriers. Breast cancer linkage consortium. Lancet 1994;343(8899):692–5.
[5] Evans DG, Shenton A, Woodward E, et al. Penetrance estimates for BRCA1 and BRCA2 based on genetic testing in a Clinical Cancer Genetics service setting: risks of breast/0 varian cancer quoted should reflect the cancer burden in the family. BMC Canc 2008;8:155.
[6] Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 and BRCA2 mutations detected in case series unselected for family History: a combined analysis of 22 studies. Am J Hum Genet 2003;72(5):1117–30.
[7] Struewing JP, Hartge P, Wacholder S, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. N Engl J Med 1997;336(20):1401–8.
[8] Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk predicition. Cancer 1994;73(3):643–51.
[9] Vasen HF, Haites NE, Evans DG, et al. Current policies for surveillance and management in women at risk of breast and ovarian cancer: a survey among 16 European family cancer clinics. European Familial Breast Cancer Collaborative Group. Eur J Cancer 1998;34(12):1922–6.
[10] Evans DG, Lalloo F. Risk assessment and management of high risk familial breast cancer. J Med Genet 2002;39(12):865–71.
[11] Gail MH, Brinton LA, Byar DP, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Nat Cancer Inst 1989;81(24):1879–86.
[12] Antoniou AC, Cunningham AP, Peto J, et al. The BOADICEA model of genentic susceptibility to breast and ovarian cancer: updates and extensions. Br J Canc 2008;98(8):1457–66.
[13] Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. Stat Med 2004;23(7):1111–30.
[14] Lalloo F, Baildam A, Brain A, Hopwood P, Howell A, Evans DGR. Preventative mastectomy for women at high risk of breast cancer. Eur J Surg Oncol 2002;26:711–3.
[15] Evans DG, Baildam AD, Anderson E, et al. Risk reducing mastectomy oucomes in 10 European centres. J Med Genet 2009;46(4). 354-258.
[16] Evans DG, Cuzick J, Howell A. Cancer Genetics Clinics Eor J Cancer 1996;32A(3). 391-391.
[17] Julian-Renier C, Eisinger F, Moatti JP, et al. Physicians' attitudes towards mammography and prophylactic surgery for hereditary breast/ovarian cancer risk and subsequently published guidelines. Eur J Hum Genet 2000;8(3):204–8.
[18] Julian-Renier C, Bouchard LJ, Evans DG, et al. Women's attitudes towards preventive strategies for hereditary breast or ovarian carcinoma differ from one country to another: differences among English, French and Canadian women. Cancer 2001;92(4):959–68.
[19] Evans DG, Kerr B, Cade D, et al. Fictitious breast cancer family history. Lancet 1996;348(9033):1034.
[20] Tercyak KP, Peshkin BN, Brogan BM, et al. Quality of life after contralateral prophylactic mastectomy in newly-diagnosed high-risk breast cancer patients who underwent BRCA1/2 testing. J Clin Oncol 2007;25(3):285–91.
[21] Evans G, Kwong A, Baildam A. The genetics of breast cancer, risk-reducing surgery and prevention. In: Dixon J, editor. Breast Surgery, a companion to specialist surgical practice. fifth ed. Saunders Elsevier Pub; 2014. p. 127–45.
[22] Jensen J, Lin J, Kapoor N, Giuliano A. Surgical delay of the nipple-areolar complex: a powerful technique to maximize nipple viability following nipple-sparing mastectomy. Ann Surg Oncol 2012;19:3171–6.
[23] Reynolds C, Davidson J, Lindor N, et al. Prophylactic and therapeutic mastectomy in BRCA mutation carriers: can the nipple be preserved? Ann Surg Oncol 2011;18:3102–9.
[24] Yao K, Liederbach B, Tang R, et al. Nipple-sparing mastectomy in BRCA1/2 mutation carriers: an interim analysis and review of the literature. Ann Surg Oncol 2015;22:370–6.
[25] Cyr A. Safely expanding the use of nipple sparing mastectomy in BRCA mutation carriers. Ann Surg Oncol 2015;22:353–4.
[26] Coopey S, Smith B. The nipple is just another margin. Ann Surg Oncol 2015;22:3764–6.
[27] Metcalfe K, Tulin D, Semple J, et al. Long-term psychosocial functioning in women with bilateral prophylactic mastectomy: does preservation of the nipple-areolar complex make a difference? Ann Surg Oncol 2015;22:3324–30.
[28] Didier F, Rdaice D, Gandini S, et al. Does nipple preservation in mastectomy improve satisfaction with cosmetic results, psychological adjustment, body image and sexuality? Breast Canc Res Treat 2009;118:623–33.
[29] Lim G, Baildam A. Novel approach for risk-reducing mastectomy: first-stage implant placement and subsequent second-stage mastectomy. Plast Reconstr Surg 2018 Sep;142(3):607–10.
[30] Fentiman I. Prophylactic mastectomy: deliverance or delusion? BMJ 1998;317:1402.
[31] Milne C. Editorial Comment - prophylactic mastectomy: deliverance or delusion? BMJ 1998;317:1402.
[32] Hartmann L, Schaid D, Woods J, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. N Engl J Med 1999;340:77–85.
[33] Hartmann L, Schaid D, Sellers T, et al. Bilateral prophylactic mastectomy in BRCA1/2 mutation carriers. American Assoc for Cancer Research; 2000.
[34] Rebbeck TR, Friebel T, Lynch HT, et al. Bilateral prophylactic mastectomy reduces breast cancer risk in BRCA1 and BRCA2 mutation carriers: the PROSE study group. J Clin Oncol 2004;22:1055–62.
[35] Hartmann LC, Sellers TA, Schaid DJ, et al. Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. J Natl Cancer Inst 2001;93:1633–7.
[36] Meijers-Heijboer H, van Geel B, van Putten WLJ, et al. Breast cancer after prophylactic mastectomy in women with a BRCA1 or BRCA2 mutation. N Engl J Med 2001;345(3):159–64.
[37] Friebel TM, Domchek SM, Neuhausen SL, et al. Bilateral prophylactic oophorectomy and bilateral prophylactic mastectomy in a prospective cohort of unaffected BRCA1 or BRCA2 mutation carriers. Clin Breast Canc 2007;7(11):875–82.
[38] Evans DG, Baildam AD, Anderson E, et al. Risk-reducing mastectomy: outcomes in 10 European centres. J Med Genet 2009;46(4):254–8.
[39] Evans DG, Anderson E, Lalloo F, et al. Utilisation of prophylactic mastectomy in 10 European centres. Dis Markers 1999;15(1–3):148–51.
[40] Baltzer HL, Alonso-Proulx O, Mainprize JG, et al. MRI volumetric analysis of breast fibroglandular tissue to assess risk of the spared nipple in BRCA1 and BRCA2 mutation carriers. Ann Surg Oncol 2014;21:1583–8.
[41] Metcalfe KA, Tulin D, Semple JL, et al. Long term psychosocial functioning in women with bilateral prophylactic mastectomy: does preservation of the nipple-areolar complex make a difference? Ann Surg Oncol 2015;22:3324–30.
[42] Brandberg Y, Sandelin K, Erikson S, et al. Psychological reactions, quality of life and body image after bilateral prophylactic mastectomy in women at high risk for breast cancer: a prospective 1-year follow-up study. J Clin Oncol 2008;26:3943–9.
[43] Gopie JP, Mureau MA, Seynaeve C, et al. Body image issues after bilateral prophylactic mastectomy with breast reconstruction in healthy women at risk fro hereditary breast cancer. Fam Cancer 2013;12:479–87.
[44] Metcalfe KA, Esplen MJ, Goel V, et al. Psychosocial functioning in women who have undergone bilateral prophylactic mastectomy. Psycho Oncol 2004;13:14–25.
[45] Lodder LN, Frets PG, Trijsburg RW, et al. One-year follow-up of women opting for presymptomatic testing for BRCA1 and BRCA2: emotional impact of the test outcome and decisions on risk management (surveillance of prophylactic surgery). Breast Canc Res Treat 2002;73:97–112.
[46] Metcalfe KA, Mian N, Enmore M, et al. Long-term follow-up of Jewish women with a BRCA1 and BRCA2 mutationwho underwent population genetic screening. Breast Canc Res Treat 2012;133:735–40.
[47] Graves KD, Vegella P, Poggi EA, et al. Long term psychosocial outcomes of BRCA1/BRCA2 testing: differences across affected status and risk-reducing surgery choice. Cancer Epidemiol Biomark Prev 2012;21:445–55.