Oncology

Evaluation of breast cancer occurrence in patients with previous in vitro fertilisation treatment

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Abstract

Introduction
Breast cancer affects mostly 50–69-year-old women, with a history of previous breast or colon cancer, subfertility, nulliparity, ionising radiation, late menopause, smoking, fatty diet and positive for malignancies family history. Researchers support the multiple, unsuccessful under in vitro fertilisation (IVF) treatment, efforts to be an aetiologic factor for the disease. The aim of this review was to evaluate the breast cancer's occurrence in correlation to previous IVF exposure for the treatment of subfertility.

Material and methods
We searched the web using several keywords, such as 'ART/IVF/breast cancer/malignancies/BRCA 1-2 mutations', and found lots of interesting articles, forums, blogs and case reports. All this data-warehouse became a very useful tool in our hands in order to proceed in the basic online analytical processing during data-mining of 86 breast cancer 'web-cases' surgically treated at least seven years after their last IVF treatment (association rules, sequence analysis, classification, clustering and forecasting regarding the type of the tumour (benign, malignant), the number of the previous IVF treatments and several involving in breast cancer factors (age, obesity, parity,

history of ovarian, breast or colon cancer, smoking)).

Results
Low cancer risk was found after IVF treatment in some studies, while other researchers observed higher malignancy rate in IVF patients compared with the risk in the general population. Several studies attributed the increased risk to the underlined pathology causing both the infertility and the malignancy, while several other scientific efforts are focused on findings proving higher rates for malignant tumours in the ART-treated patients. We noticed that this controversy is attributed to the lack of a systematic and worldwide-accepted classification in the cancer patients, who have undergone IVF treatment(s), in terms of several factors: age, body weight, parity, previous breastfeeding, habits and positive for malignancies history. Studies on these factors and their coactions in the malignant breast behaviour after IVF exposure should precede any data processing in order for the latter to become scientifically fertile.

Conclusion
If we classify the IVF-candidate women in terms of their personal and family history, we will find a way out of this controversy and eventually, minimise the various potential long-term breast malignant complications in IVF treatment through adequately informing our general population.

Introduction

Breast cancer affects mostly 50–69-year-old women, with a medical history of fatty diet, previous ovarian, breast or colon cancer, subfertility[1], nulliparity[2], ionising radiation, late menopause, smoking

and a positive for malignancies family history[3]. Several researchers support the multiple, unsuccessful under IVF treatment, efforts to be another aetiologic factor for the disease[4]. The literature frequently reveals cases of hormone-dependent breast carcinoma in patients with previous IVF treatment[5], while the authors of these case reports often question themselves whether such an oestrogen-dependent cancer is strongly related to the extended ovarian stimulation or not[3]. The latter has already become a current controversy on the matter: Is there any link between breast cancer and IVF treatment? This review evaluates breast cancer occurrence in patients with previous IVF treatment.

Material and methods

We investigated in the worldwide web (data-warehouse: articles, forums, case reports; data-mining: sequence analysis, association rules, classification, clustering, forecasting) for related matters, applying several keywords such as 'IVF/breast cancer/malignancies/BRCA 1-2 mutations', etc. and we came across many articles and examined several forums, blogs and case reports (focusing mostly on cases with tumours surgically extracted at least seven years after previous IVF treatment(s)). We investigate the several cited aspects and their analysis on the issue in question and found an adequate number of interesting articles with sometimes totally opposed opinions. All the above data-warehouse became a very useful tool in our hands so as to proceed in the basic online analytical processing (measures: data with mean values, categorisation/dimensions (like: age,

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obesity, parity, previous breast, ovarian or colon cancer, etc.))[6], in datamining, such as the association rules (method for discovering interesting relations between variables within large databases)[7], the sequence analysis (comparison of sequences in order to find similarities, identification of intrinsic sequence features or sequence differences, etc.)[8], the classification (identifying the subpopulation to which new observations belong)[9], the clustering (assignment of a set of observations into subsets (called clusters) so that observations in the same cluster are similar in some sense)[10], the forecasting (process of making statements about events whose actual outcomes (typically) have not yet been observed)[11] for breast cancer cases after previous IVF treatment. All this statistical procedure was particularly valuable in forming an integrated icon for the matter in question and furthermore, in creating a proper strategy for taking correct decisions on the application of any needed IVF therapy in our patients, accompanied at the same time by a deep scientific interest on the minimisation of the breast cancer's occurrence.

Results

The extraction of information is based on web-material, which we found scientifically interesting, using several criteria such as quality and traffic of the website, impact factor of medical magazines, etc. However, since human bias[12] can never be excluded from the experiments, our conclusions remain safe only to the degree that we accept the restrictions of the researcher's human nature. Another difficulty was the labourious task needed to adequately detect the variety of the factors, which had been potentially mentioned in the collected web-texts analysed in our study.

Discussion

We studied 86 web-cases (with breast tumour surgically treated at least seven years after their last IVF treatment) and classified them according to the type of their tumour (benign, malignant), the number of previous IVF treatments and some of the involving to breast cancer factors (age, obesity, parity, history of breast, ovarian or colon cancer). An overall online analytical processing table is shown below (Table 1).

Table 1

The above table was the outcome of all the tables that we had initially worked on and moreover, revealed various corelations hidden among different values/dimensions. An association rules' example is cited below (Table 2).

Table 2

We noticed that fat women (BMI >27 kg/m^2) were more eligible in developing a breast malignancy even with only one previous IVF effort, compared to the corresponding ones who had been treated for benign tumours. Moreover, medical history of previous breast, ovarian or colon cancer was present in malignant cases >35 years old, with >1 previous IVF treatment. Consequently, sequence analysis and association rules can enlighten us on our observations to make the proper clustering and classification, essential tool in forecasting and safe selection of IVF candidates. Medical literature presents huge controversies concerning the issue breast malignancies' occurrence in patients with previous IVF treatment. On the one hand, a significantly low cancer risk was found after IVF in several studies[13,14], while on the other hand, many researchers have observed a higher rate of malignancy in IVF patients compared with the known risk in the general population[15]. We noticed that this extended spectrum of scientific attitude towards this controversial theme is mainly attributed to the lack of a systematic and a worldwide-accepted classification (low and high risk for cancer patients, undergoing IVF treatment) according to several

Table 1 Tumours appeared and surgically extracted at least seven years after previous IVF treatment(s)									
		Age		Obesity (mean value during the years after the last IVF therapy)		Parity		Previous breast, colon or ovarian cancer	
		<35 years old	>35 years old	BMI <27 kg/m^2	BMI >27 kg/m^2	0 or one child	>1 child	(+) positive	(-) negative
Benign tumour	One IVF treatment	7	14	5	7	10	5	2	11
	>1 IVF treatment	10	26	9	16	11	24	4	22
Malignant tumour	One IVF treatment	3	7	2	2	2	8	2	8
	>1 IVF treatment	5	14	5	5	13	8	6	13

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Table 2 Tumours appeared and surgically extracted at least seven years after previous IVF treatment(s)		Age		Obesity (mean value during the years after the last IVF therapy)		Parity		Previous breast, colon or ovarian cancer	
		<35 years old	>35 years old	BMI <27 kg/m²	BMI >27 kg/m²	0 or one child	>1 child	(+) positive	(-) negative
Benign tumour	One IVF treatment		+		+	+		+	
	>1 IVF treatment	+							
Malignant tumour	One IVF treatment	+							+
	>1 IVF treatment		+				+	+	
Benign tumour	One IVF treatment	+							+
	>1 IVF treatment		+	+					
Malignant tumour	One IVF treatment	+			+				
	>1 IVF treatment		+			+		+	
Benign tumour	One IVF treatment	+		+					+
	>1 IVF treatment		+				+		
Malignant tumour	One IVF-treatment		+		+	+		+	
	>1 IVF treatment		+			+			

factors for malignancies like age, body weight, parity, positive for malignancies family history, etc. Studies, concerning each of these factors and their coactions in the potential future malignant breast behaviour after IVF exposure, must precede any further data processing of the above-mentioned research in order for the latter to become scientifically fertile.

Conclusion

We strongly support that an integrated approach on the matter in question must be followed by applying on the one hand, the principles of audit in the existing studies (meta-analysis, cohort, etc.), so as a reasonable assurance that the collected information is free from material error, while on the other hand, new surveys must be conducted on the basis of a proper classification, concerning the risk factors that involve in the development of the breast malignancy. By reviewing previous research and by conducting new surveys under a correct and satisfying classification, like the one mentioned above, an order will be established in the sector of IVF treatment, minimising at the same time its various complications such as the new potential breast cancer cases. Only if we classify the IVF-candidate women according to their personal (age, obesity, parity, medical history of previous cancer, etc.) and family (breast or ovarian cancer, colon malignancies, etc.) history in low and high risk for future cancer development patient-categories, we will find a way out of this great controversy and we will eventually minimise the several potential long-term complications, such as breast tumours, in IVF treatment through adequately informing/consulting our general population.

Review

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