

Indocyanine green utility in prevention and treatment of breast lymphedema

Nicolae BACALBASA^{1,2}, Radu ZAMFIR³, Irina BALESCU⁴, Roxana BOHILTEA^{1,5}, Sorin PETREA⁶, Sorin ALDOESCU⁶, Mihaela VILCU^{6,7}, Iulian BREZEAN^{6,7}, Lucian POP⁸, Alexandru CIULCU⁹, Dragos ROMANESCU¹⁰, Claudia STOICA^{11,12}, Cristina MARTAC¹³, Bogdan URSUT^{7,14}, Alexandru FILIPESCU^{1,15}, Cezar Laurentiu TOMESCU^{16,17}, Adnan Ad ALOUL^{18,19}

¹ Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

² Department of Visceral Surgery, Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

³ "Dan Setlacec" Center of Gastrointestinal Disease and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania

⁴ Department of Visceral Surgery, "Ponderas" Academic Hospital, Bucharest, Romania

⁵ Department of Obstetrics and Gynecology, "Filantropia" Clinical Hospital, Bucharest, Romania

⁶ Department of Surgery, "Dr.I. Cantacuzino" Clinical Hospital, Bucharest, Romania

⁷ Department of Surgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁸ Department of Obstetrics and Gynecology,

"Alessandrescu-Rusescu" National Institute of Mother and Child Care, Bucharest, Romania

⁹ Department of Obstetrics and Gynecology, "Dr.I. Cantacuzino" Clinical Hospital, Bucharest, Romania

¹⁰ Department of Surgery, "Sanador" Clinical Hospital, Bucharest, Romania

¹¹ Department of Anatomy, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

¹² Department of Surgery, Ilfov County Emergency Hospital, Bucharest, Romania

¹³ Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania

¹⁴ Department of Surgery, "Agrippa Ionescu" Clinical Emergency Hospital, Bucharest, Romania

¹⁵ Department of Obstetrics and Gynecology, "Elias" Emergency Hospital, Bucharest, Romania

¹⁶ Department of Obstetrics and Gynecology, "Ovidius" University of Medicine and Pharmacy, Constanta, Romania

¹⁷ Department of Obstetrics and Gynecology, "Sf. Andrei" Clinical Emergency Hospital, Constanta, Romania

¹⁸ Department of Surgery, Ramnicu Sarat County Hospital, Buzau, Romania

¹⁹ Department of Surgery, "Titu Maiorescu" University, Bucharest, Romania

ABSTRACT

Breast cancer represents the most commonly encountered malignancy in women worldwide. In the last decades, due to the improvement of the imagistic techniques and to the wide implementation of screening tests, a significant number of cases are suitable for conservative surgery therefore improving the quality of life. Although the postoperative morbidity after breast conservative surgery is reduced, the procedure can still be associated with certain complications such as breast lymphedema, or wound difficult healing. The aim of the current paper is to discuss the possibility of prevention and treatment of breast lymphedema by using innovative techniques such as indocyanine green.

Keywords: breast cancer, conservative surgery, breast lymphedema, indocyanine green

Corresponding authors:

Irina Balescu

E-mail: irina.balescu@ponderas-ah.ro

Roxana Bohiltea

E-mail: r.bohiltea@yahoo.com

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INTRODUCTION

Breast cancer represents the most commonly encountered neoplastic disease in women, accounting for almost 12% of all newly diagnosed cancers; meanwhile this malady seems to be responsible for up to 6,6% of all cancer related deaths, mortality being especially related to the stage at the time of diagnosis (1). Fortunately, in the last decades imagistic techniques gained significant progress and led to an earlier diagnostic of the disease in a significant number of cases, therefore increasing the chances for cure in breast cancer patients. In this respect, surgeons' attention was focused on imaging and less invasive surgical procedures in order to offer a better cosmetic aspect and an improved quality of life without diminishing the quality of the surgical procedure and without impeding the oncological aspects (2,3). Therefore, conservative surgery such as quadrantectomy has been proposed especially in cases presenting small in size lesions. According to the clinical, histopathological and imagistic aspects of the axillary lymph nodes, the therapeutic strategy of the axilla was de-escalated from axillary lymph node dissection to sentinel lymph node dissection. In time both quadrantectomy and sentinel lymph node dissection have been widely adopted by the international breast cancer guidelines and therefore became the new standard of care especially in reduced lesions with no suspect axillary lymph nodes (4,5).

THE ROLE OF INDOCYANINE GREEN ADMINISTRATION IN SENTINEL NODE DETECTION

In order to minimize the chances to misdiagnose the real sentinel lymph node, multiple methods have been proposed for a more accurate identification; the most commonly used agent for sentinel lymph node detection is still represented by Technetium. However, Technetium administration is also associated with certain risks, being a radioactive molecule; in this regard, attention was focused on determining which other agents could be useful in such cases (6-10). Methylene blue has proved its efficacy, but after injection, local necrosis can develop and special attention should be paid (7). A more recently used molecule is represented by indocyanine green (ICG), a fluorescent molecule which absorbs light between 600nm and 900 nm and emits fluorescence between 750 nm and 950 nm (11). Once the utility of ICG has been demonstrated in order to provide a more effective detection of sentinel lymph node, attention was focused on identifying other possible utilities of this agent. Due to the fact that it can be easily identified in the blood and lymphatic stream, the molecule has been also used in order to prevent and

treat different complications such as lymphedema (11-13).

WHY DOES BREAST LYMPHEDEMA OCCUR AFTER CONSERVATIVE BREAST SURGERY?

Breast lymphedema has become a serious problem affecting women undergoing breast conservative surgery; this fact is mainly related to the interruption of breast lymphatic network during surgery, leading to an impeded breast lymphatic drainage; in this context fluid stasis at the level of the breast will lead to the apparition of inflammatory response which will further have a negative impact on the subcutaneous tissues; therefore local architectural modification and breast lymphedema will occur leading to a predisposition for cellulitis development as well as to a negative impact on patients' body image (14-17). In the last decade, due to the extensive implementation of breast conserving surgery, breast lymphedema has become an important problem, especially due to the fact that most often these patients are submitted to adjuvant radiation therapy, which might further worsen the local situation (17).

When it comes to the incidence of breast lymphedema after conservative surgery, the reported rates range between 10% and 70% due to the fact that most often the diagnosis is based on clinical identification; however, it should not be omitted the fact that clinic is most often based on a subjective interpretation (18). Although certain authors proposed imagistic methods such as mammography and ultrasound, these methods fail to identify with a high sensibility and specificity the development of breast lymphedema (19,20).

THE ROLE OF INDOCYANINE GREEN IN BREAST LYMPHEDEMA

A significant improvement in the field of breast lymphedema diagnostic was achieved by the association of intraoperative lymphography based on indocyanine green injection; the method allows a better identification of the lymphatic map of the breast. The method is based on the same principle as the one described for preventing upper limb lymphedema (19).

An interesting study which was conducted on the subject of indocyanine green utility in diagnostic of breast lymphedema was conducted by Heydon-White et al. which has been recently published in Breast Cancer Research and Treatment journal. The study included 10 healthy controls and 10 patients presenting breast lymphedema after breast conserving surgery. In all cases indocyanine injection was administrated intra-

dermally in three standard points. The study came to demonstrate that in controls the amount of liquid was significantly lower when compared to cases submitted to breast conserving surgery; however, in the affected breast a significantly higher amount of liquids was encountered at the level of the lower quadrants when compared to the upper ones as well as at the level of the inner ones when compared to the outer quadrants. Performing an indocyanine green based lymphography came to demonstrate that 90% of cases who had been submitted to breast conserving surgery presented collateral pathways of drainage at the level of the parasternal, intercostal, clavicular or contro-lateral axilla, the latter type of drainage being more commonly encountered in cases in which ipsilateral lymph node dissection had been performed. For the time being, all patients presenting breast lymphedema had dermal backflow in the affected breast, aspect which was not encountered in the control group. According to the authors, indocyanine green lymphography in such cases could provide an early diagnostic of breast lymphedema, before it becomes clinically visible and could also

determine the therapeutic strategy before irreversible changes develop (21). Moreover, other authors suggest that indocyanine green lymphography is able to identify the areas presenting a significant overload of the lymphatic system and might create in this way the premises of creating a lymphatico-venous anastomosis in order to decrease the pressure into the lymphatic system by discharging the accumulated amount of lymph directly into the venous system (22).

CONCLUSIONS

Once screening tests have been implemented worldwide, the rates of early breast cancer diagnosis significantly increased and therefore more patients are candidates for conservative surgery. Although this type of surgery is usually associated with better cosmetic aspects and an improved quality of life, certain complications such as breast lymphedema might occur. In such cases indocyanine green injection seems to be safe and effective in both prevention and treatment this complication.

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