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Understanding variations in the use of hypofractionated radiotherapy and its specific indications for breast cancer: A mixed-methods study

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ABSTRACT

Background and purpose: Radiation oncology guidelines favour hypofractionated whole-breast radiotherapy (HWBRT) over more conventional schemes in the conservative treatment of breast cancer, but its adoption still varies in clinical practice. This study assessed the patterns of HWBRT adoption in Catalonia (Spain).

Material and methods: We used a mixed-methods approach based on an explanatory sequential design, first collecting and analysing quantitative data on HWBRT use (>2.5 Gy per fraction) in 11 public radiotherapy centres (2005–2015) and then performing 25 semi-structured interviews with all department heads and reference radiation oncologist/s.

Results: Of the 34,859 patients fulfiling the study criteria over the study period, just 12% were hypofractionated, reaching a percentage of 29% in 2015 ($p < 0.001$). Our analysis showed a narrowing age gap between patients receiving conventional fractionation and hypofractionation in centres leading adoption. However, there were important differences in clinicians' interpretation of evidence (e.g. regarding the perceived risk of long-term toxicity) and selection of patients for specific indications, both within and between departments.

Conclusions: Differences observed in the rate of adoption of HWBRT could not be tackled only using a rational, evidence-based approach. Factors related to the management of radiotherapy departments play a major role in the diffusion of therapeutic strategies.

A consolidated body of evidence [1–4] has shown that a high proportion of breast cancer patients may achieve the same clinical outcomes with 15–16 fractions (40–42.5 Gy) of postoperative radiotherapy as with the longer conventional radiotherapy course of 25 fractions. Randomized studies show that this conservative regimen is more convenient for patients, incurs a lower cost for the healthcare system, and causes less acute skin toxicity [5]. From a cancer care policy standpoint, the American Society for Radiation Oncology (ASTRO), the European Society for Radiotherapy & Oncology (ESTRO), and the National Institute for Health and Care Excellence (NICE) all prefer the so-called *modest hypofractionation* (2–3 Gy per fraction) [6] for most patients with early breast cancer, recognizing the positive implications for health systems with high caseloads of patients potentially undergoing such regimen. Indeed, hypofractionation schedules reduce acute toxicity, which can lead to discontinuation of radiotherapy treatment [7]. Despite the benefits for patients and health systems and its consideration as a standard of care [8,9], hypofractionated whole-breast radiotherapy (HWBRT) still encounters resistance, and its adoption varies in clinical practice [10,11].

Although other strategies—such as breast-intensity modulated radiotherapy (IMRT)—have been adopted on the basis of less

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evidence and higher cost [12], some authors argue that randomized evidence and published guidelines alone are not sufficient grounds to adopt HWBRT [10]. Past discussions regarding tumour-grade sensitivity to hypofractionation [13,14], the unclear effect of biological sub-types in the efficacy of the hypofractionated schedule [8], or breast reconstruction [15] might be contributing to the slow path of adoption and limited utilisation. Caution is still warranted in patients under 40 and in those receiving primary systemic treatment [16] or regional node irradiation (RNI) [17]. Thus, particularly in a context in which the regional clinical guideline does not specifically address this issue [18], departments may interpret evidence for specific indications and nonclinical factors differently, which would explain the existing variability in its adoption.

Our study aims to provide an overview of the adoption of hypofractionation for breast cancer in the Public Health Service of Catalonia (Spain). We combine quantitative and qualitative approaches to evaluate the evolution of its use from 2005 to 2015 and to explain the data from the perspective of radiation oncologists involved in breast cancer treatment in the region.

Materials and methods

We used a mixed-methods approach based on an explanatory sequential design, which consists of two different interactive phases [19,20]. First we collected quantitative data on hypofractionation use; in light of the wide variation of our results, we added a qualitative study in radiotherapy departments. Exploring participants' views in depth helped to explain statistical results by both disentangling the specific indications described at each department and the clinical rationale behind them [21]. Our final interpretation and analysis considered the interaction between quantitative and qualitative findings [22]. The reasons for mixing quantitative and qualitative methods were *completeness* for a more comprehensive account of the area of inquiry and *discovery* of hypotheses [19].

We assessed the use of hypofractionation for the 11 public radiotherapy centres in Catalonia (Spain), which provide oncology treatments for a population of 7.5 million and comprise a total of 35 linear accelerators. The longest distance between the home of an individual requiring radiation treatment in Catalonia and a facility is 170 km, while 80% of the population lives within 20 km. The cost of treatments is reimbursed on the basis of four levels of complexity, regardless of the fractions used.

Quantitative assessment

We assessed the use of hypofractionation for patients receiving breast cancer treatment with a curative intent in 2005–2015, using data from the Catalonian Hospital Reimbursement Database, which includes all patients receiving a course of radiotherapy. It collects data on sex, age, radiotherapy centre, aim of treatment, tumour site, total dose, planning system, initiation and finalisation of treatment, and number of sessions. It is mandatory to fill out for reimbursement. The criterion for radiotherapy to be considered hypofractionated was >2.5 Gy per fraction. The doses included in this study ranged from 2.67 to 3.00 Gy. We assessed differences in patterns of use with descriptive statistics and logistic regression, using SPSS (version 21.0, 2012) and STATA (version 12) software.

Qualitative assessment

The qualitative study consisted of 25 semi-structured on-site interviews held in October–December 2015 with all department heads and reference breast cancer radiation oncologist/s at each hospital. One-on-one interviews ensured that all critical points were addressed, and the 45–60 min sessions were flexible enough to enable participants to volunteer information on topics relevant to them. Only at the end of each interview was provided anonymised information about the centre's HWBRT utilisation relative to other centres (Figs. 1 and 3). The evaluation of HWBRT, with no comparative information, allowed us to limit the risk of information bias and to contribute to the internal validity of the study based on strictly local perspectives from each service. All interviews were audio-taped and transcribed [23]. These data were then compiled into a documentary record and rendered anonymous.

To analyse the data, we applied thematic-analysis criteria, which emphasise the meaning of the text and interpret its thematic content [24,25]. After checking saturation of information [26], we read through to identify general themes and thematic categories to ensure interpreter consensus. We compared interviews to capture recurring views and related experiences [27]. A systematic process of data-treatment analysis was facilitated by the use of the Atlas-ti 6.2 software [28]. Coding and interpretation consistency was checked during analysis by reviewing the transcripts at different moments in time.

Results

Quantitative assessment

Of the 34,859 patients fulfiling the study criteria, only 4,322 (12.4%) breast cancer patients received hypofractionation in the 11 public radiotherapy departments in Catalonia in 2005–2015, with important variations in use across departments ($p < 0.001$). In 2015, 29% of patients received hypofractionated radiotherapy (table 1). While the scheme (2.67–3.0 Gy) ranged from 1% to 36.6% in 2010 among different departments, these figures rose to 8.9% and 74.7% in 2015 (Fig. 1). The use of hypofractionation in 2015 exceeded 50% in two departments, while another five used the therapy 25–50% of the time, and four others less than 25% of the time.

Likewise, the median age of patients in 2015 appeared relevant when deciding the regimen to be applied; the more hypofractionation is used, the smaller the age difference between patients who receive it and those who don't (Fig. 2). By contrast, patients' age was near or over 70 years in the four departments with lower rates of HWBRT use.

The trends in the adoption of hypofractionation varied significantly by department, and in several individual cases we observed a striking, non-linear behaviour (Fig. 3). Three milestones in this time period frame the observed variability from a health system perspective. First, three centres (1, 2 and 9) introduced hypofractionation in routine practice in 2008 and 2011, in one case it had completely superseded the conventional scheme by 2015. Second, 2014–2015 seemed a turning point for many departments in the adoption of hypofractionation, and 4 out of 11 showed utilisation rates near 30%. Finally, by 2015, there were still four centres using the technique less than 25% of the time, highlighting wide differences in use between centres.

Qualitative assessment

The results of the quantitative assessment can be interpreted in light of the criteria determining the use of hypofractionation in each department. We analysed criteria concerning clinical factors emerging from the interviews on the basis of specific indications and created three categories to describe the use of hypofractionation in each department as *physician-dependent*, attributable to *most professionals* (including the reference ones for breast cancer), or with higher degree of homogeneity: a *unified practice* (Fig. 4).