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Letters

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Letter to the Editor: Prostate Cancer. An Insight into Screening and Local Treatment

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JAMES AND Glaholm [1], in the October issue of the *European Journal of Cancer*, provided an overview of the questions to be studied and to be solved about prostate cancer. We would like to make some comments concerning screening and local treatment. There has indeed been an explosion in the diagnosis of prostate cancer in men over 55, not only in the United States but also in Europe. The reason is due to the more and more frequent practice of serum PSA (prostate specific antigen) determination by general practitioners and urologists, followed by endorectal ultrasonography and guided biopsies. For example, in the Department of Isère (France), there has been a significant increase in incidence (crude rate) between 1979 and 1990 ($P = 0.001$) from 22.1 to 45 per 100 000 men without any change in the rate of prostate cancer death; the onset of the increase coincides with the use of PSA [2]. So far, there is no consensus to recommend individual screening in men from 55 to 70, and we are eager to see the results of the ongoing mass screening programmes to know whether or not screening and treating early stage cancers will decrease the death rate.

Such testing has radically modified the clinical stages of the diagnosed cases which correspond in more than 70% of the cases to stages T12NXM0 [3]. It has been convincingly demonstrated that prostate cancer progresses in all men but is not always fatal; not all men with localised prostate cancer need treatment, and some people consider that only men with a life expectancy of 10 years of more and patients with poorly differentiated cancers deserve a treatment with curative intention [4]. We need to know what should be offered to the patient who is found to be positive on an individual screening.

A randomised trial comparing radiotherapy, total prostatectomy and watchful waiting has been recently launched by the MRC (Medical Research Council) for patients classified as T1–T2, and requires a target sample size of 1800 patients. Being included in such a trial might be hard to accept for some patients. After having agreed to be screened, these patients would be included, after another informed consent, in a trial to determine what must be done in the years to come. Nevertheless, PSA detected cancers (stage T1c) have clearly been shown not to be insignificant cancers in the vast majority of patients. In an initial series of more than 40 T1c cancer patients that underwent radical prostatectomy [5], T1c constituted approximately 35% of all radical prostatectomy candidates. In 85% of these, a significant prostate cancer was found on pathological examination of the radical prostatectomy specimen, either because of the volume of the tumour or because of the degree of differentiation. This means that of all PSA detected tumours, 15% could be considered as being insignificant. It is worthwhile noting that 35% of the patients had extracapsular disease (pT3) and that in 10%, the surgical margins were invaded. These pT3 patients, due to perforation of the capsule, or an involvement of the seminal vesicles or positive margins, have an increased risk of local (and/or systemic) relapse: an ongoing joint study from the Genito-urinary and Radiotherapy EORTC Group, which has already included more than 300 patients, is aiming to assess the role of postoperative irradiation versus delayed radiotherapy in case of local relapse, with regard to local control and survival [6]. As to definitive radiotherapy, conventional external irradiation has to be progressively replaced by three-dimensional conformal radiotherapy, which could represent a major breakthrough. The preliminary results are very promising because this technique improves significantly disease-free survival when compared to conventional radiotherapy ($P < 0.005$) [7] and enables radiation oncologists to increase the dose without increasing grade 3 and 4 acute or late toxicity [8].

The role of endocrine therapy in the local control of the disease and in disease-free survival (PSA-free survival) by radiotherapy or radical prostatectomy is being addressed. Endocrine therapy has been shown to be successful in obtaining control of locally advanced prostate cancer with external irradiation as reported in two RTOG randomised trials. A short course of neoadjuvant endocrine therapy with flutamide and goserelin continued during radiotherapy enhances both local control ($P < 0.001$) and progression-free survival ($P < 0.001$) [9]. Endocrine therapy, in a long-term adjuvant setting, with goserelin started at the end of external irradiation and to be continued indefinitely improves local control ($P < 0.001$) and progression-free survival ($P < 0.001$) [10]. Another randomised trial from the EORTC has shown that endocrine therapy with an LHRH (luteinising hormone relasing hormone) analogue, given for 3 years in T3T4 prostate cancer, started at the onset of irradiation, increases local control and disease-free survival ($P = 0.001$) [11]. Neoadjuvant endocrine therapy followed by radical prostatectomy has now been reported to decrease significantly the number of positive surgical margins in T1 and T2 prostate cancer [12, 13]. Its role in T3 cancer is still questionable, but pT3 prostate cancer can be cured in some cases where negative surgical margins can be obtained [13]. Nevertheless, the timing and the duration of neoadjuvant endocrine therapy in combination with surgery or radiotherapy for localised prostate cancer has to be studied further [14].

Prostate cancer has changed its face and is mostly detected in curable stages. Randomised trials comparing the different treatment strategies are very unlikely to recruit successfully enough patients to give us the right answer. A watchful waiting policy in patients with early prostate cancer and a significant expected survival does not seem acceptable; tumour pro-

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gression will occur and the chance of curing extracapsularly extending disease will be compromised. The future will probably show that only by curing cancer can the probability of dying from it be decreased; the toxicity of surgery or radiotherapy has decreased in terms of mortality and morbidity of bladder, digestive tract and sexual function. The locoregional therapeutic approach has to remain multidisciplinary between pathologists, urological surgeons and radiation oncologists, using the same criteria of clinical staging, therapeutic evaluation and quality of life, all the more as the diagnosis is made at an earlier stage. Medical information has to be shared with general practitioners to enable patients to have the same perception of their disease. In the future, we need to learn more from the biomolecular approach which could enable us to adapt local and adjuvant treatments according to the tumour phenotype.

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Male Breast Cancer: Statistical and Clinical Data for the Maltese Population

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THE MALTESE Islands have a population of approximately 350000 and occupy an area of 316 km^2. They are situated in the centre of the Mediterranean Sea. Data on male breast cancer is very limited and we are not aware of any data ever being presented for Malta [1–3]. Data for this series has been collected through our National Cancer Registry within the department of Health, and is therefore a very reliable source of information. Between 1980 and 1995, a total of 13 male breast cancer cases were diagnosed and registered amongst the male population which stands at 183550, as of the end of 1992.

The crude incidence rate 1990–1995 was 0.8 per 100000. The age-adjusted (World Standard) incidence rate was 0.54 (95% confidence interval 0.44–0.64). The age-adjusted (World Standard) sex ratio, female versus male, was 70.1. The median age at diagnosis was 69 years and it was observed that these rates increased sharply with age. The cumulative risk increased consistently with age (0–74). Thus, in the absence of other causes of death, a male in Malta has an estimated 0.05% risk of developing male breast cancer before the age of 75 years. There was one recorded death in the male population due to breast cancer. The age-adjusted (World Standard) mortality rate was 0.46 per 100000.

Clinically, all these patients were managed on the same lines as adopted for female breast cancer [4–5]. It is quite justified to draw inferences in this way, as the data on this rare tumour is very limited.

All 13 patients underwent a modified radical mastectomy. The histology was reported as being invasive adenocarcinoma in 10 cases and of ductal carcinoma in the remaining 13 cases. For these 13 cases, the pathological staging T of TNM was available; 10 cases were T3 and 3 cases were T1. N was also available; 8 had N1 and 4 cases were N0. There were no cases of distant metastasis at the time of diagnosis. In comparison with other published series, there was no notable variation in pathological findings [6–8].

Among these male breast cancer cases, there was a particular case with a family history of female breast in daughters and sister of the proband [9]. We are now proceeding with more detailed analysis at molecular level, screening DNA for mutations in *TP53, BRCA1* and *BRCA2* in all cases as well as in relatives of the particular case [10].

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