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# The idiosyncratic relationship between diagnostic delay and stage of oral squamous cell carcinoma

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## KEYWORDS

Oral squamous cell carcinoma;  
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**Summary** Approximately half of patients with oral cancer present with advanced lesions when five-year survival rates are as low as 20%, however, diagnostic delay has repeatedly been found to be unrelated to the stage of oral cancer at diagnosis. The aim of this study was to investigate why diagnostic delay is frequently unrelated to the stage of oral cancer at diagnosis. The odds ratio (OR) of early versus advanced oral squamous cell carcinoma was calculated for 245 consecutive patients with untreated oral squamous cell carcinoma. Being female (OR = 0.40; 0.19–0.80;  $p < 0.05$ ) and married (OR = 0.27; 0.11–0.66;  $p < 0.01$ ) was predictive of early stage disease. Being non-white (OR = 5.42; 1.66–17.67;  $p < 0.01$ ) was predictive of advanced stage disease. There is no evidence that these patient demographics are associated with faster growing tumours, yet it is possible that those who are male, unmarried and non-white may not notice an oral lesion until it is advanced in stage. It is concluded that differences in tumour biology are not a likely explanation for the absence of a delay–stage relationship but instead, a proportion of tumours may be silent until advanced in stage.

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## Introduction

Oral cancer has a five-year survival rate of 50% or less.<sup>1,2</sup> This rate is much improved when lesions are diagnosed at an early stage of the disease (i.e. small and localised), with five-year survival

rates of up to 90% when lesions are less than 2 cm in size.<sup>3</sup> In fact, clinical stage at the time of diagnosis is one of the most important and accurate prognostic indicators for oral cancer.<sup>4–6</sup> Furthermore, detecting oral cancer at an early stage is believed to be the most effective means to reduce morbidity<sup>7</sup> and duration of treatment.<sup>8</sup> However, up to half of patients with oral cancer present with advanced lesions<sup>9</sup> when five-year survival rates are as low as 20%.<sup>1,3</sup> If the proportion of patients

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presenting with advanced stage disease can be reduced, it is reasonable to assume that the results of treatment would improve.<sup>10</sup> To facilitate early diagnosis it is important that the factors pre-disposing to advanced stage are identified.

A possible explanation for the high incidence of advanced stage oral cancer is prolonged diagnostic delay (the time interval between the first recognition of symptoms and a definitive diagnosis). In support of this hypothesis, studies in breast cancer patients have demonstrated that prolonged diagnostic delay is associated with increased tumour size and advanced stage of disease at diagnosis.<sup>11</sup> However, diagnostic delay has repeatedly been found to be unrelated to the stage of oral cancer at diagnosis<sup>12,13</sup>

Two reasons have been suggested to explain this phenomenon. Firstly, there may be intrinsic differences in tumour aggressiveness which determine the tumour size and stage at diagnosis<sup>10,14,15</sup> (Fig. 1). The premise being that biologically aggressive tumours will grow to an advanced stage after only a short period of delay, due to the pace of tumour growth. Conversely, patients with slow growing tumours may have early stage disease at diagnosis even after a substantial period of diagnostic delay.

The second explanation suggests that although the stage of disease at diagnosis will be reliant

upon the time interval between the *onset of disease* and a definitive diagnosis, some oral cancers may be silent in that they may be asymptomatic at the onset of the disease and in its early stages<sup>10,14</sup> (Fig. 2). In turn, it is possible that tumours may go unrecognised by patients until they are at an advanced stage.<sup>16</sup> Conversely, alert patients may identify signs or symptoms of oral cancer when it is pre-neoplastic or early stage disease. As the pre-neoplastic phase can extend over a long period of time<sup>1,12</sup> prolonged diagnostic delay may have minimal impact on the stage of disease at diagnosis. This scenario could explain why some patients are found to have early stage disease even though they have experienced prolonged diagnostic delay.

The primary aim of the current study was to investigate the relationship between diagnostic delay and stage of disease to determine which of the two explanations is more plausible. To do this, the study endeavoured to identify factors associated with early versus advanced stage of disease. There is no evidence that demographic factors are associated with faster growing tumours. In turn the 'tumour aggressiveness hypothesis' would be supported if patient demographics were found to be unrelated to the stage of disease at diagnosis. On the other hand, it is possible certain demographic

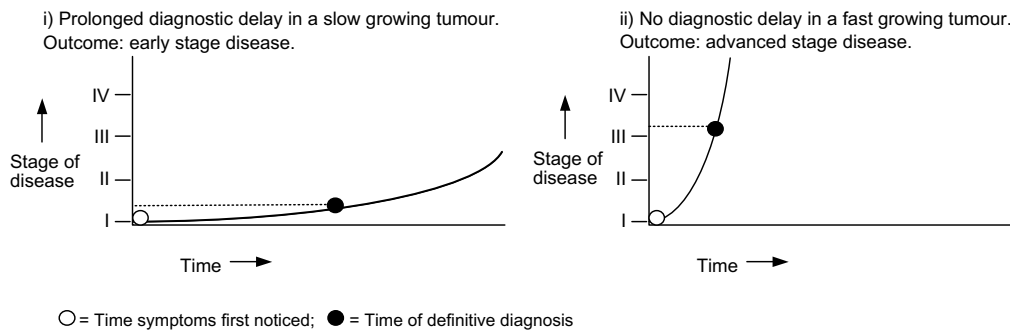


Figure 1 Tumour aggressiveness hypothesis: some tumours are more aggressive than others.

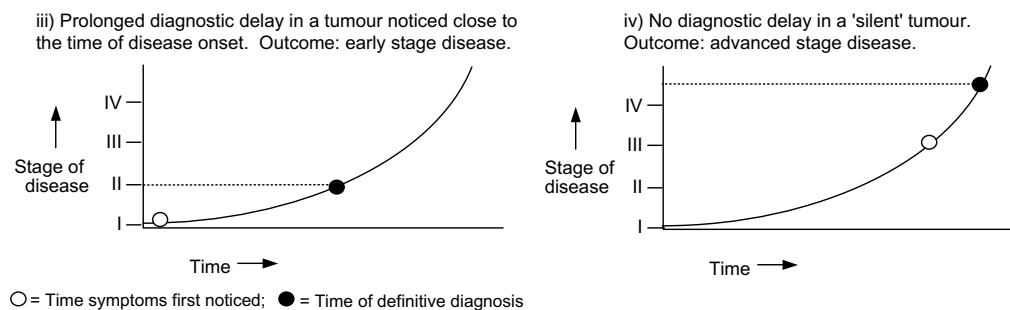


Figure 2 Silent tumour hypothesis: patients do not necessarily notice symptoms at the onset of disease.

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