

## Commentary

# Comments on the article of Bu, et al entitled “P16<sup>INK4a</sup> overexpression and survival in osteosarcoma patients: a meta analysis”

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In the recent, with great interest we read the article “P16<sup>INK4a</sup> overexpression and survival in osteosarcoma patients: a meta analysis” (by Bu J et al). In this study, the investigators performed a meta-analysis to provide a comprehensive evaluation of the significance of P16<sup>INK4a</sup> expression in patients with osteosarcoma. This article showed that patients with high P16<sup>INK4a</sup> expression were significantly associated with favorable overall survival when compared to low or undetectable P16<sup>INK4a</sup> expression. The investigators concluded that P16<sup>INK4a</sup> is an effective biomarker of survival for osteosarcoma patients [1]. It is a valuable study. Nevertheless, there're some flaws existing in this meta-analysis that we would like to raise.

Firstly, the sources of included studies were not appropriate. Investigators only systematically searched relevant articles in four databases: Pub Med, Embase, Web of Science and CNKI. The small number of required articles would bring great bias to the results. We suggest they could search more electronic databases to get more eligible studies. Moreover, the investigators searched CNKI database, a Chinese database not usually used in meta-analysis and at least five of the eight included articles were got from this database. We wonder why these investigators did not use a more commonly-used database, such CBM database and Wan Fang database, to ensure they would not omit eligible studies in this article.

Secondly, as we all know, search process of search strategies plays an important role in meta-analysis. However, in this article, the investigators didn't clearly describe search process of search strategies report for databases, and didn't show how many articles they retrieved and how they excluded other articles. It is generally suggested that the search process should be showed as a flow chart but I didn't find this kind of chart in this article.

Thirdly, some important detailed characteristics of the eight studies were ignored in this meta-analysis. For example, case number, number of patients with high/low level of P16<sup>INK4a</sup>, age, sex, follow-up, osteosarcoma classification, pathological parameter, country and other information were not provided. We think that follow-up is very important information for survival rate calculation/assessment of patients with osteosarcoma. We hope the investigators could provide us these data in this article, which are helpful for readers to better understand the results.

Fourthly, the investigators did not assess the quality of each article. It is well known that articles of high-quality are necessary for a meta analysis. Low-quality article may bring wrong and harmful conclusion. Even though methods of quality assessment about clinical controlled trials are controversial, quality assessment is still necessary. In this paper, I saw no information mentioned about the quality of each study.

Fifthly, seven studies reported data on the 3-year overall survival [2-8], and only one study reported to data on the 5-year overall survival [9]. We wonder why these investigators did not conduct a subgroup analysis to evaluate the significance of P16<sup>INK4a</sup> expression in 3-year overall survival of patients with osteosarcoma.

In a word, we agree that P16<sup>INK4a</sup> is an effective biomarker of survival for osteosarcoma. However, the small sample size may inevitably increase the risk of bias. Therefore, more large scale clinical trials are needed to further identify the prognostic significance of P16<sup>INK4a</sup> for osteosarcoma.

#### Disclosure of conflict of interest

None.

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