Eighth edition of the American Joint Committee on Cancer staging system for soft tissue sarcoma of the trunk and extremity: in search of a better staging system

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The American Joint Committee on Cancer (AJCC) staging system is one of the most widely used cancer staging systems worldwide. The AJCC staging system for bone and soft tissue sarcoma (STS) has been revised to the 8th edition in 2017 (1).

The following are the primary changes in the 8th edition of the AJCC staging system for STS:

(I) up to the 7th edition, the same stage classification was used regardless of the anatomical occurrence sites of STS (2). In the 8th edition, different staging systems are adopted depending on the anatomical sites of STS. In the STS staging, the tumor sites are divided into four categories: (i) trunk and extremity; (ii) retroperitoneum; (iii) head and neck; and (iv) abdomen and thoracic visceral organs. However, the prognostic stage groups of STSs in the latter two categories are not defined;

(II) regarding STS of the trunk and extremity, a tumor with regional lymph node metastasis without distant metastasis (anyTN1M0anyG) is classified as stage IV in the 8th edition. In the 7th edition, anyTN1M0anyG was defined as stage III;

(III) in the 7th edition, T factor was divided into two categories: T1, ≤5 cm and T2, >5 cm. However, in the 8th edition, T factor is classified into four categories: T1, ≤5 cm; T2, >5 and ≤10 cm; T3, >10 and ≤15 cm; and T4, >15 cm.

As a result, stages IA and IB have not been changed, stage IIA in the 7th edition has been retained to stage II in the 8th edition, and stage IIB in the 7th edition has been changed to stage IIIA in the 8th edition. Stage III in the 7th edition has been divided into stages IIIA for T2 tumor and IIIB for T3 and T4 tumors in the 8th edition depending on the tumor size. Furthermore, anyTN1M0anyG has been changed from stage III in the 7th edition to stage IV in the 8th edition. STS with distant metastasis was not changed to stage IV in both editions.

To validate whether the AJCC staging for STS of the trunk and extremity is a better staging than the 7th edition by revising it to the 8th edition, the significance of the classification of anyTN1M0anyG as stage IV and the divide of tumor size into four categories should be evaluated. The recent study by Fisher *et al.* has attempted to answer such questions (3).

Fisher *et al.* have used the registry data of more than 1,500 Commission on Cancer accredited facilities obtained from the National Cancer Database (NCDB) of the United States. The NCDB data cover 70% of patients with newly developed cancer in which 24 million data of patients with cancer have been registered since 1985. They obtained a large number of data about 26,144 patients aged 18 years or older with STS of the trunk and extremities from the database, and the patients were classified using the 7th and 8th editions to examine the validity of the staging of the 8th edition and to analyze the prognosis of each stage.

The hazard ratios (HRs) of the risk of death based on each stage in the 7th edition was 1.2 for stage IB, 1.4 for IIA, 1.6 for IIB, 3.6 for III, and 14.1 for IV with stage IA as the

reference. By contrast, the HRs of the risk of death in the 8th edition were 1.2 for stage IB, 1.4 for II, 2.6 for IIIA, 4.0 for IIIB, and 14.1 for IV with stage IA as the reference. In stage IV, the HRs were 6.2 for M1 and 15.3 for N1M0. The risk of death increased as the stage increased, indicating that both editions of the staging system are effective.

However, in the 7th edition, a large incremental increase in HR was observed between stages IIB and III, whereas such increase was noted between stages IIIA and IIIB in the 8th edition. In the 8th edition, when evaluated according to 5-year overall survival (OS), OS rates were as follows: stage IIIA, 62.4%; IIIB, 50.1%; stage IV N1M0, 33.1%; and M1, 12.4%. The 5-year OS of N1M0 was significantly better than that of M1 (P<0.001) and significantly worse than localized disease (P<0.01). When evaluating T factor, the 5-year OS rates of T1 and T2 in the 7th edition were 78.8% and 58.8%, respectively, and T2 tumor had a significantly poorer prognosis (P<0.01). In the 8th edition, the 5-year OS rate of T2 was 62.6%, indicating a significantly worse prognosis than T1 (P<0.01). However, the 5-year OS rates of T3 and T4 were 53.5% and 56.1% respectively, and no significant difference was observed (P=0.52).

Since anyTN1M0 is classified as stage IV in the staging systems of most cancers, its classification as stage III in the 7th edition of the AJCC staging system for STS may have caused confusion. In the 8th edition, anyTN1M0 is restored to stage IV as in the 6th edition. However, the study by Fisher *et al.* has suggested that the prognosis of anyTN1M0 was somewhat similar to stage IIIB than M1 in terms of the HR of the risk of death and almost in between IIIB and M1 in terms of the 5-year survival rate. Given the significant difference between N1M0 and M1 in terms of HR, it is difficult to conclude whether it was reasonable to reclassify N1M0 to stage IV in the 8th edition. Considering the balance with other cancer types, N1M0 is easier to understand as stage IV. However, it may be more appropriate to set N1M0 as stage IVA and M1 as IVB.

By contrast, regarding T factor, which is divided into four categories, the validity of T3 and T4 could not be confirmed based on the results of the Fisher *et al.*'s study; rather, it might be better to classify T factor into three categories by defining a tumor larger than 10 cm as T3.

Other study similar to that of Fisher *et al.* has also been reported by Cates using 21,396 patients aged 18 years or older with STS of the trunk and extremities obtained from the Surveillance Epidemiology and End Results (SEER) database (4). Unlike the study by Fisher *et al.*, that of Cates has used disease-specific survival rather than OS; thus, it is difficult to directly compare the results of both studies. However, concerns about the reclassification of N1M0 and M1 into stage IV and T factor into four categories were again raised. Cates has also concluded that the 8th edition was no better than the 7th edition.

Fisher and colleagues have also examined the validity of the 8th edition of the AJCC staging system for retroperitoneal STS using the NCDB data (5). Although T factor is divided into four categories as in the case of STS of the trunk and extremity, no significant difference was observed in terms of prognosis from T1 to T4, indicating that the prognosis of retroperitoneal STS could not be predicted with T factor alone. Moreover, the survival curves of retroperitoneal STS were not clearly divided based on each stage as those of the trunk and extremity. These observations suggest that it would be significant to separate the staging system of STS according to the anatomical sites. In the future, the staging system corresponding to each anatomical site must be optimized.

Alongside the AJCC staging, the widely used cancer staging system is the Union for International Cancer Control (UICC) TNM classification. For STS of the trunk and extremity, anyTN1M0anyG is classified as stage IIIB in the UICC 8th edition, which is similar to the 7th edition and is defined as stage IV in the AJCC 8th edition (6). By contrast, for retroperitoneal STS, anyTN1M0anyG is retained as stage IIIB both in the UICC and AJCC staging 8th edition. Thus, it is necessary to pay close attention to how such dissociation between UICC and AJCC staging systems for STS of the trunk and extremity will be resolved.

The prognosis of STS will change with the times as the treatment and diagnostic technology advances. Based on the study by Fisher *et al.*, it is considered an extremely important and useful method in verifying the validity of the staging system by fitting previous cases to the current stage classification. At the same time, data must be prospectively obtained and used as a basis for planning future staging, and constant efforts are needed for the development of a better staging system for STS.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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