Acute Postoperative Frailty

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We read with great interest the article by Dr Wolfe concerning the influence of surgical stress on muscle mass in the elderly. The author underlines that the catabolic response to stress is of even greater concern in the elderly, because of the limited muscle mass of many older people before injury and operation.1 Wolfe also suggests that hormonal therapy together with nutritional supplementation and exercise can represent a possible strategy to prevent the catabolic response and improve physical function after operation.

We agree with the author. But some additional issues need to be addressed. A major focus of research in clinical geriatrics is frailty syndrome, a clinical entity characterized by a vicious cycle in which sarcopenia plays a central role.2 Hormonal dysregulation (decline in anabolic hormones and increase in catabolic hormones) and inflammation (increased levels of inflammatory cytokines), often through a synergistic interaction, are important pathways to frailty.2,3 Several authors have proposed that frailty becomes clinically evident at the time of acute stress.2

Major surgical stresses, such as coronary artery bypass grafting with cardiopulmonary bypass, are examples of such triggers and are followed by an acute inflammatory response and hormonal changes that have been related to hemodynamic and metabolic effects. We recently investigated alterations in anabolic and catabolic hormones occurring after coronary artery bypass grafting in older patients4 in 19 patients (12 men and 7 women) aged 70.1 ± 6.1 years (age range 62 to 80 years) with coronary artery disease who underwent cardiac operation. Cortisol, dehydroepiandrosterone, luteinizing hormone, estradiol, total testosterone, sex hormone-binding globulin, and insulin-like growth factor-1 were measured the day before, on the day of the procedure, and 1, 2, 3, and 4 days after operation. We found a substantial decrease in serum insulin-like growth factor-1 levels along with increased levels of cortisol, dehydroepiandrosterone, and estradiol in both men and women. A dramatic drop in serum testosterone levels (< 200 ng/dL, considered a cut-off for hypogonadism) was also observed in older men after operation.5 Reduction in anabolic hormones such as testosterone and insulin-like growth factor-1 can be explained and can also contribute to an increase in inflammatory cytokines, such as interleukin (IL)-6, tumor necrosis factor-α, IL-1β, a chain of events that can lead to sarcopenia after operation.2,3 In addition, inflammation plays an important role in muscle catabolism.2 All these findings support the intriguing notion proposed by Wolfe suggesting that administering an anabolic hormone before, during, and immediately after operation can actually reduce postoperative complications.

Testosterone is a good candidate for replacement therapy in older men having an operation because, in addition to its anabolic effects on skeletal muscle, well described by Ferrando and colleagues6 it can negatively modulate inflammatory cytokines.7 Our group recently found an important inverse association between serum testosterone and IL-6 soluble receptor in an older male population, which was independent of potential confounders. The presence of soluble IL-6 receptor expands the repertoire of cells that respond to IL-6 signaling, enhancing the biologic activity of IL-6.8 Guler and coauthors9 studied 25 adult men who received a coronary stent. Testosterone enanthate (IM once a week for 3 weeks) considerably attenuated the increment in C reactive protein and IL-6 that commonly occurs after the stenting procedure. In accordance, testosterone enanthate (100 mg/week) in 27 hypogonadal men for 1 month substantially reduced circulating levels of the other two important inflammatory cytokines (tumor necrosis factor-α and IL-1β) and increased IL-10 levels (an antiinflammatory cytokine).7

In conclusion, surgical stresses are followed by increased inflammation and hormonal dysregulation. In the elderly, this stress is superimposed on the already altered hormonal
mikrovec and preexisting mild proinflammatory state and sarcopenia. We are grateful to Dr Wolfe for emphasizing the importance of this topic in the older population. The premises are good. The time for a randomized clinical trial to test this hypothesis has arrived.

REFERENCES

Level IV Neck Dissection in Laryngeal Carcinoma

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I read with great interest the article, “Do pathologic and molecular analyses of neck dissection specimens justify the preservation of level IV for laryngeal squamous carcinoma with clinically negative neck?” by Dr Elsheikh and colleagues. The authors present an interesting and important observation on critical issues concerning level IV node metastasis of laryngeal carcinoma. I am particularly concerned about the conclusion made in this article, stating, “Using immunohistochemistry and in addition, developing the genetic diagnosis of occult metastases, we shall probably discover that selective neck dissection (IIA, III) is justified for patients with supraglottic and glottic squamous carcinoma with a clinically N0 neck, and transglottic and primary subglottic tumors will also require level IV dissection.” The authors also stated, “So, level IV dissection may not be necessary for supraglottic and glottic tumors in N0 necks. But transglottic and primary subglottic tumors may well require level IV dissection.” It is well known that transglottic carcinoma represents a group of glottic cancers that include paraglottic space invasion. Clinically, transglottic carcinoma usually crosses Morgagni’s ventricle in a vertical plain and involves glottic and supraglottic sites. It is sometimes possible, but not always, for a transglottic cancer to involve subglottis. Khafif and coworkers reported on 71 patients, including 42 with supraglottic primary and 29 with transglottic primary cancers, who underwent neck dissections, which included levels II and IV in all patients. They found that of 43 patients who underwent elective lateral neck dissection, the only 1 (2.3%) with level IV metastases also showed metastases at level II. Nine (32%) of the other 28 patients with clinical adenopathy had level IV metastases. They concluded that dissection of level IV as part of a therapeutic neck dissection for supraglottic and transglottic squamous cell carcinoma is recommended for patients with clinically enlarged lymph nodes, but its necessity in the absence of detectable adenopathy is challenged.

I agree with the authors that “Lymphatic collectors of the supraglottic and glottic larynx drain primarily into level II and secondarily into level III cervical lymph nodes; the lymhatic vessels of the subglottic drain primarily into level IV lymph nodes.” But I postulate that the patients who have transglottic cancer with metastatic level IV nodes either have other metastatic nodes at levels II and III or have subglottic invasion. I wonder if a transglottic cancer without subglottic invasion or clinically enlarged nodes will also require level IV dissection.