Impact and Timing of Bilateral Adrenalectomy for Refractory ACTH-Dependent Cushing Syndrome

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Background: Reluctance to perform bilateral adrenalectomy (BA) for ACTH-dependent Cushing syndrome (CS) from an untreatable primary source may result in worsening metabolic derangements and increased adverse events (AE). We hypothesized that post-BA patients would have better metabolic parameters and fewer deaths due to steroid excess than patients treated with steroidogenesis inhibition (SI) alone.

Methods: Data from patients with ACTH-dependent CS from an uncontrollable source treated between 1970-2012 were retrospectively reviewed by treatment group (SI or SI+BA). Validated severity scales were used to calculate a metabolic (M) score (hypokalemia, hyperglycemia, hypertension, proximal muscle weakness) and an AE score (thrombosis, fracture, infection, treatment-related AEs).

Results: 65 patients were included (16 pituitary, 49 ectopic); 21 (32%) were treated with SI+BA and 44 (68%) with SI alone. Presenting M scores and source of ACTH excess (ectopic vs. pituitary) were similar, but SI+BA patients had lower initial AE scores (p=0.04), likely due to selection bias. Both groups improved metabolically after treatment. However, post-SI+BA patients with resolution of CS had significantly lower M and AE scores than post-treatment scores in SI pts (p=0.02, p=0.01). SI+BA patients received SI pre-BA for a median of 7.8 mos (range 0.8-46.4). Of the SI+BA patients who had AE between presentation and BA, 39% occurred within 12 mos after presentation. 24 (55%) of SI patients died with a median survival of 24.0 mos; steroid excess contributed to 71%. Six deaths (29%) occurred in the SI+BA group; 3 of the 18 patients (17%) with sustained resolution of CS died of cancer-related causes (median 7.1 mos after BA). The others were alive at median follow up of 32.4 mos. Three patients had recurrent CS after BA (14%); all 3 died (2 related to steroid excess) at a median of 33.0 mos follow up. Minor perioperative complications occurred in 7 patients.

Conclusions: Post-treatment M and AE scores improved for SI, and to a greater extent, SI+BA patients. More than a third of AEs occurred in SI+BA patients preoperatively within 12 mos of presentation, emphasizing the importance of early surgical intervention. In addition, BA was associated with minimal complications. The majority of deaths in the SI group were related to steroid excess. Most SI+BA patients experienced sustained resolution of CS after BA; the few deaths in this group were related to primary disease. These data argue for the safety and efficacy of early BA in selected patients with uncontrollable CS.