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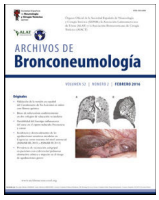

Editorial

Central Airway Stenosis: Opening the Path

Estenosis de la vía aérea central: abriendo el camino

Central airway stenosis (CAS) is a pathological condition which leads to airflow limitation of the trachea, main stem *bronchi*, *bronchus intermedius* or a *lobar bronchus*. It is a common and serious clinical problem that affects both adults and children and is widely believed to be under-diagnosed.

Several factors concerning the underlying disease and the patient's health status will define an individualized diagnostic and therapeutic approach.[1]

Multiple classification systems have been proposed during the last 30 years, most of them focused on surgical approaches and in outcomes based on treatable anatomic premises, excluding extensions beyond the trachea and the possibility of endoluminal treatment.[2–4] In 2007, Freitag et al. published the first classification system designed to grade tracheobronchial stenosis from a Pulmonologist's perspective.[5] In 2010, Murgu and Colt suggested a different classification, based on both qualitative and quantitative criteria.[6]

It seems necessary to standardize nomenclatures and find descriptors that include the degree of stenosis, patient's functional status, histologic and morphologic types, extension, localization and mechanisms of obstruction.

CAS can arise from congenital or acquired conditions. It may result from intrinsic stenosis or extrinsic compression, causing a fixed obstruction; or by cartilage or pars membranous flaccidity, leading to a dynamic obstruction. Numerous clinical conditions are identified, but nowadays malignant disease outnumbers benign diseases, especially due to the increase in primary lung cancer, as well as metastatic pulmonary disease. Historically literature reported that 20–30% of patients with lung cancer will develop CAS. A most recent study shows a prevalence of 13% at lung cancer diagnosis, with a further 5% of patients developing CAS within a year.[7]

The presentation symptoms can be insidious and may be obscured for a long time resulting in a delayed diagnosis and worst outcome. They will depend on the location, extend and degree of obstruction, speed of progression and underlying disease. Early manifestations may be mistaken for other diseases such as asthma or COPD. Main symptoms are usually dyspnea and stridor, occurring in 54% of patients as initial complain.[8] They are more prominent during exercise but may progress to dyspnea at rest. The first occurs when airway lumen is reduced to 8 mm and the second when it reaches less than 5 mm. Cough, wheezing, diminished sputum clearance and recurrent infections will emerge when it reaches this severity.

Clinical investigations for the underlying diagnosis include computed tomography, with 97% sensitivity for extra thoracic compression[9]; dynamic CT is effective for the diagnosis of tracheobronchomalacia and excessive dynamic airway collapse. Flow-volume loops may provide information regarding the level and degree of obstruction but a plateau is only reached after severe lumen impairment.[10] These exams have not yet substituted flexible bronchoscopy as the primary procedure for diagnostic work-up and pre-interventional assessment since it provides a direct view of the airway.

In the therapeutic decision, according to Galluccio et al., the most important differentiation is between simple and complex stenosis because it determines the success or failure of the endoscopic intervention.[11] Surgical management remains the preferred approache but there are situations in which, whether due to patient's limitation or the nature of the pathology, interventional bronchoscopy, with techniques such as laser, cryotherapy, mechanical dilation or debridement, play a preponderant role.

Airway stents are placed to maintain airway patency. They are indicated in both intraluminal and extraluminal major CAS and can be used in both benign and malignant disease. The decision to place an airway stent is balanced between capacity of prevention the airway reocclusion and long-term complications associated.

When it comes to the choice of the stent, several considerations must be taken in account, as a plethora of many different stents from various materials, sizes and shapes are available. Silicone stents are cheaper, easily retrievable and can be repositioned as much times as necessary. On the other hand, they need rigid bronchoscopy to be handled, are more suitable to migrate and interfere with mucociliary clearance. Nitinol stents can be placed by flexible bronchoscopy and are usually more adaptable to an irregular surface. Based on 2005 Food and Drug Administration warning, metallic stents are not recommended in benign airway strictures because of the reported extensive granulation tissue and stent fracture. The ideal stent should be simple to insert, easily removable, capable to resist compression, allow clearance of secretions, easy to nail to avoid migration and would match the shape of stenotic airway (but is does not exist yet).

A recent evolutional step was made when manufacturers offered modifications of their products according to patient's needs, with

rapid prototyping 3D printing techniques, allowing stents to be tailored to the individual's airway. In reference centers, these stents can be printed in days, or even hours, but a totally personalized airway stent with specific angles, widths and length would take several weeks to be prepared, which is not acceptable when rapid symptomatic relief is necessary.[12]

Bioabsorbable airway stents, made of different biomaterials, are under investigation and have been deployed in humans. Polydioxanone is the one that has been most used and the longest reported time free of intervention was 44 months.[13] Other compounds are under analysis like polylactic acid, polyglycolic acid, polycaprolactone, polyurethane or polyamide.[12,14,15]

In our group, we are using an experimental polycaprolactone (PCL)/hydrogel polymer stent coated with umbilical cord mesenchymal stem (UCMSC) cells and dental pulp stem cells (DPSC) mesenchymal stem cells. Preliminary results of *in vitro* MSC's static seeding and dynamic seeding are very promising, and we are now starting animal testing.

Although it is expected an exciting new generation of personalized airway stents along with stem cell therapy, this reality is far to be achieved. If on one hand 3D printing technology could become accessible for physicians, on the other hand there are no certified manufacturers nor a direct access between parts. Maybe a creation of a software easy-to-use between hospitals and manufacturers could provide that answer. Several legal problems will emerge such as how to get authorization from governments or what official entities should regulate this process.

Meanwhile, this dialog must go on.

References

1. Stratakos G, Gerovasili V, Dimitropoulos C, Giozos I, Filippidis FT, Gennimata S, et al. Survival and quality of life benefit after endoscopic management of malignant central airway obstruction. J Cancer. 2016;7:794–802.
2. Cotton RT. Pediatric laryngotracheal stenosis. J Pediatr Surg. 1984;19:699–704.
3. Grundfast KM, Morris MS, Bernsley C. Subglottic stenosis: retrospective analysis and proposal for standard reporting system. Ann Otol Rhinol Laryngol. 1987;96:101–5.
4. Myer CM 3rd, O'Connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol. 1994;103:319–23.
5. Freitag L, Ernst A, Unger M, Kovitz K, Marquette CH. A proposed classification system of central airway stenosis. Eur Respir J. 2007;30:7–12.
6. Colt HG, Murgu SD. Interventional bronchoscopy from bench to bedside: new techniques for early lung cancer detection. Clin Chest Med. 2010;31:29–37.
7. Daneshvar C, Falconer WE, Ahmed M, Sibly A, Hindle M, Nicholson TW, et al. Prevalence and outcome of central airway obstruction in patients with lung cancer. BMJ Open Respir Res. 2019;6:e000429.
8. Casas DB, Fernández-Bussy S, Folch E, Flandes Aldeyturriaga J, Majid A. Non-malignant central airway obstruction. Arch Bronconeumol (Engl Ed). 2014;50:345–54.
9. Fishman AP, Elias JA. Fishman's pulmonary diseases and disorders. McGraw-Hill Medical; 2008.
10. Bugalho A. Management of subglottic stenosis and subglottic stenosis in systemic disease. In: Principles and practice of interventional pulmonology. Springer; 2013. p. 409–20.
11. Galluccio G, Lucantoni G, Battistoni P, Paone G, Batzella S, Lucifora V, et al. Interventional endoscopy in the management of benign tracheal stenoses: definitive treatment at long-term follow-up. Eur J Cardiothorac Surg. 2009;35:429–33.
12. Freitag L, Gördes M, Zarogoulidis P, Darwiche K, Franzen D, Funke F, et al. Towards individualized tracheobronchial stents: technical, practical and legal considerations. Respiration. 2017;94:442–56.
13. Lischke R, Pozniak J, Vondrys D, Elliott MJ. Novel biodegradable stents in the treatment of bronchial stenosis after lung transplantation. Eur J Cardiothorac Surg. 2011;40:619–24.
14. Tatekawa Y, Kawazoe N, Chen G, Shirasaki Y, Komuro H, Kaneko M. Tracheal defect repair using a PLGA–collagen hybrid scaffold reinforced by a copolymer stent with bFGF-impregnated gelatin hydrogel. Pediatr Surg Int. 2010;26:575–80.
15. Tsukada H, Matsuda S, Inoue H, Ikada Y, Osada H. Comparison of bioabsorbable materials for use in artificial tracheal grafts. Interact Cardiovasc Thorac Surg. 2009;8:225–9.

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