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# Bronchospasm and iodinated contrast media (ICM): an accurate evaluation is mandatory

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## KEY WORDS

*Bronchial asthma; bronchospasm; iodinated contrast media; hypersensitivity; psychological stress.*

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## Doi

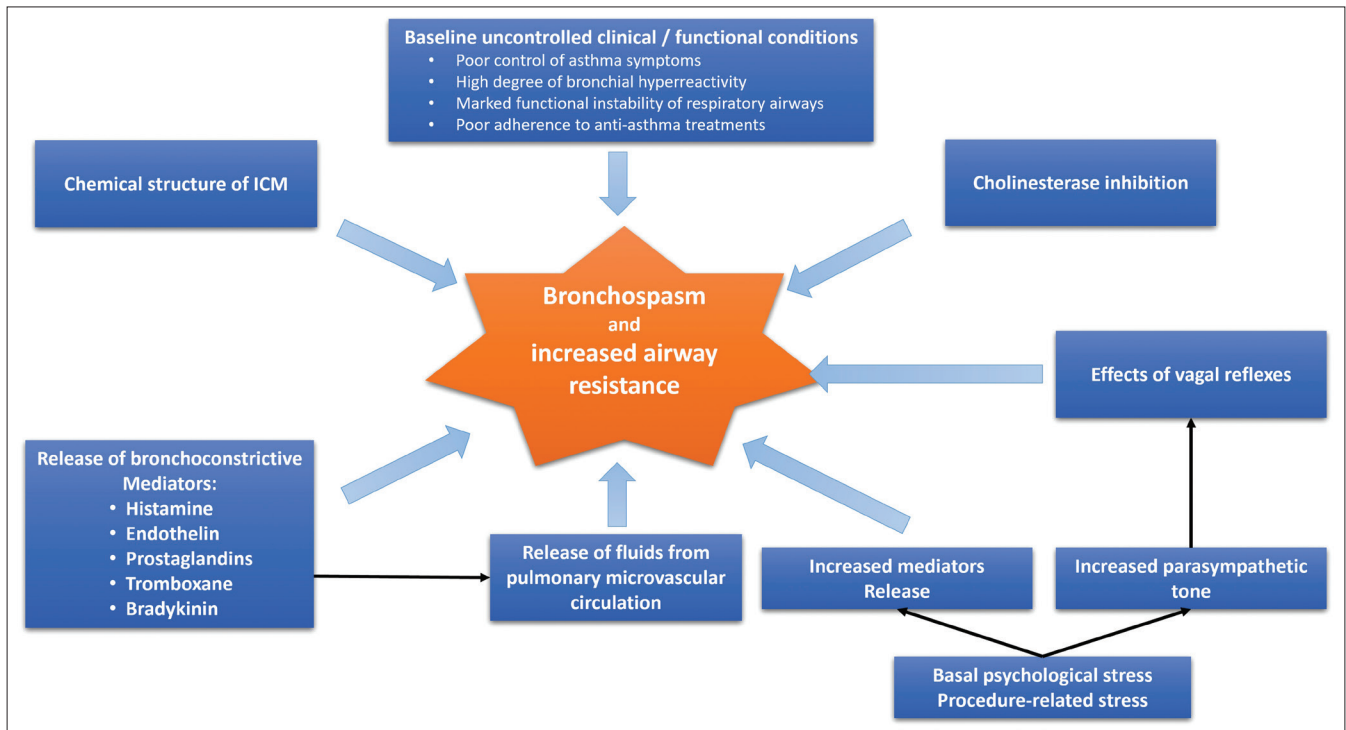
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To the Editor,

we have greatly appreciated the editorial *Iodinated contrast media hypersensitivity reactions: is it time to re-evaluate risk factors?* (doi: 10.23822/EurAnnACI.1764-1489.245) and three articles about the relevant topic of hypersensitivity reactions to iodinated contrast media (ICM), published on *European Annals of Allergy and Clinical Immunology* on March 2022 (*Hypersensitivity reactions to iodinated contrast media in Italy: a retrospective*

*study. Characteristics of patients and risk factors* – doi: 10.23822/EurAnnACI.1764-1489.225; *Isn't it time to consider oncological status as a new risk factor of iodinated contrast media hypersensitivity?* – doi: 10.23822/EurAnnACI.1764-1489.242; *Anaphylactic shock to iodinated contrast media: not so rare after all* – doi: 10.23822/EurAnnACI.1764-1489.210).

With this letter we wish to stress 1) the importance of respiratory symptoms (with or without concomitant manifestations) as adverse events to ICM, and 2) the need for an accurate clini-

**Figure 1** - Factors and mechanisms increasing the risk of ICM induced bronchospasm in asthmatics.

Modified from Liccardi *et al.* (15).

cal evaluation of asthmatics undergoing radiological procedures with ICM, aiming at 3) deciding when and which preventive pharmacological approach should be recommended.

We consider bronchospasm as a respiratory adverse event to ICM. According to the Ring and Messmer scale commonly adopted for reaction severity, respiratory symptoms are included into II and III grade and are associated to other multiorgan clinical manifestations (1-4). However, bronchospasm can be the only or prevalent symptom in particular circumstances, particularly in non-controlled asthma (5). Moreover, asthma severity is a risk factor for acute adverse events to contrast agents (6), and this is true also within Step 1 of GINA classification. The apparently unexplainable higher risk in Step 1, reported by Kobayashi *et al.* (6), could be justified by the fact that their study enrolled much more GINA Step 1 asthmatics than patients belonging to the other Steps and, above all, none of them were taking inhaled corticosteroids. On the contrary, from a general point of view, there is a direct correlation between the degree of asthma severity and female sex, and the risk of developing anaphylactic reactions (7). Lung is a key target for water soluble ICM, and this is reflected by bronchospasm, that constitutes the most common adverse event, among respiratory reactions, to ICM (8), with a reported occurrence of 23% and 5% cases of moderate and severe reac-

tions, respectively (9). Although symptomatic/severe bronchospasm seems to be rare, sub-clinical bronchospasm assessed by a fall in FEV<sub>1</sub> values is quite common, particularly in patients with an history of allergy and/or asthma (10). Furthermore, a bronchospasm can develop both during systemic reactions (*e.g.*, IgE/non IgE-mediated anaphylaxis) and as isolated events (10). Although low osmolar ICM have been reported to induce a reduced frequency of bronchospasm, Wilson and Davies (11) found that both high osmolar and low osmolar non-ionic ICM produce a comparable fall in FEV<sub>1</sub> and FVC, the latter an expression of air trapping (theoretically more dangerous). Other studies have shown percentages of bronchospasm between 0.18 and 4% with non-ionic ICM for computer tomography and fluorescein angiography, and also with magnetic resonance contrast medium (RCM)-gadolinium chelates (12).

The pathogenesis of ICM-induced bronchospasm is complex and not completely understood, but it is likely that this could be multifactorial (**figure 1**): the chemical structure itself, the release of bronchoconstrictor mediators (such as histamine, endothelin, prostaglandins, thromboxane and bradykinin), and the cholinesterase inhibition may play a role (13). Some of these released mediators can also cause leakage of fluids from the lung microvasculature which further contributes to increase airways

resistance (13). Recently, the role of stress as predisposing/trig-  
gering factor in asthma has been extensively studied. Individuals  
with stress due to psychological disorders or to the fear of ICM  
administration might experience vagal hypertone and, conse-  
quently, increased risk of bronchospasm (14).

An accurate evaluation of respiratory status is of essence. De-  
spite this well-known relevance of respiratory adverse events to  
ICM, little attention has been paid by healthcare professionals  
to the risk of bronchospasm in allergic/asthmatic patients re-  
quiring ICM. In fact, no recent articles have been published on  
this topic to suggest diagnostic evaluations or pharmacological  
preventive treatments (e.g.,  $\beta_2$  agonists), with consequent poor  
awareness about this risk.

This is true either in inpatient care (and, consequently, in the  
controlled environment of the hospital setting) and in outpa-  
tient care (e.g., private radiology centers).

Bearing in mind the risk of potentially fatal respiratory adverse  
events, all patients suffering from persistent (moderate/severe)  
bronchial asthma should undergo an accurate evaluation, before  
ICM administration. This should include a thorough clinical  
assessment, ideally performed by pulmonologists/allergists or  
by internists trained in respiratory medicine, aimed at optimiz-  
ing asthma control (15), as it is likely that an optimal control  
of asthma symptoms could be useful in reducing the risk of  
bronchospasm in asthmatic patients (8). Evaluation of Asthma  
Control Test (ACT) score could be very useful to detect uncon-

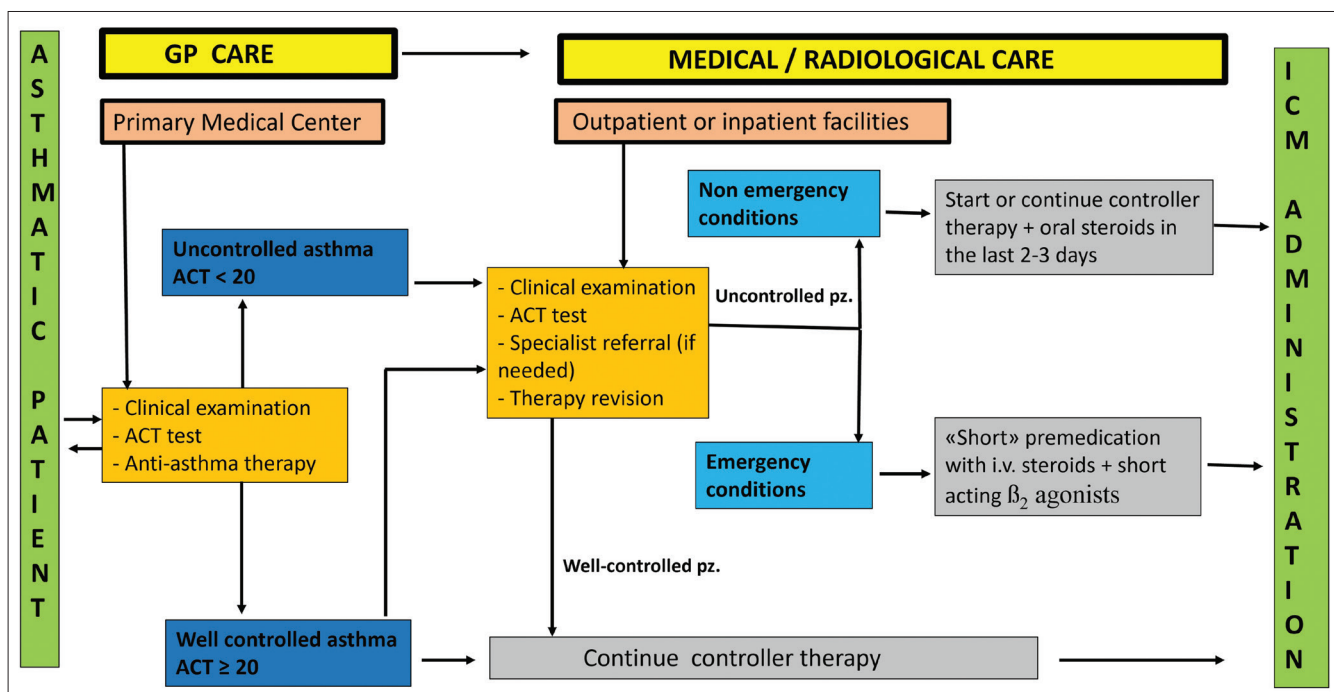
trolled patients potentially at higher risk of bronchospasm. In  
patients suffering from seasonal allergic asthma the examination  
with ICM could be postponed, if possible, outside the peak of  
the pollen season or after adequate pharmacologic treatment.

Approach to prevent ICM-induced bronchospasm is needed. Pa-  
tients at risk of respiratory adverse events should be treated with  
an optimal anti-inflammatory and reliever therapy to reduce bron-  
chial hyperreactivity and consequently the risk of bronchospasm.  
It is likely that subclinical bronchospasm might determine great-  
er obstructive effects in airways of asthmatics with uncontrolled  
asthma (11). Although uncontrolled asthma, does not represent  
a contraindication to perform ICM administration in emergency  
setting, it is quite likely that ICM administration would be safer  
in asthmatic patients that are usually well-controlled, during their  
daily life, when it is possible to perform a clinical evaluation and  
stepping up the therapy in case of poor control.

For this reason, general practitioners (GP) play an important  
preventive role, as they manage asthmatic patients in “Real  
Life”, leveraging on their long-term knowledge of patients’  
medical history and their constant commitment in managing  
and following up their chronic conditions (16). This high level  
of knowledge of the specific patient cannot be reached by the  
radiologist, as he/she may have just one single contact with the  
patient (i.e., when the radiologic procedure is performed) (16).

Figure 2 shows a possible flow-chart for the management of the  
risk of ICM – induced bronchospasm, for different healthcare

Figure 2 - Suggested flow-chart (from GP to radiologist/internist) in managing asthmatic patient before ICM administration.



professionals and settings (GPs, radiologists, and pulmonologists/internists, working in inpatient or outpatient care).

It is well known that asthmatic patients undergoing administration of water soluble ICM have an increased risk of potentially severe bronchospasm. It has been shown that the most important risk factor for bronchospasm is represented by a high degree of bronchial hyperreactivity with airway instability, not adequately controlled by long-term anti-inflammatory treatments. Therefore, an accurate clinical evaluation of asthmatics (especially those with a relevant degree of asthma severity) should be recommended, before ICM administration. Guidelines shared by pulmonologists, allergists and radiologists should be developed in the future for a better evaluation and management of these patients.

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None.

### Contributions

All authors contributed equally to this work.

### Conflict of interests

The authors declare that they have no conflict of interests.

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