Catatonia: Treatment and prognosis

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INTRODUCTION

Catatonia is a behavioral syndrome marked by an inability to move normally despite full physical capacity to do so. The syndrome occurs in the context of many psychiatric and general medical disorders [1]. Prompt treatment of catatonia with benzodiazepines or electroconvulsive therapy (ECT), as well as treatment of the underlying cause, generally leads to remission of catatonia. However, failure to recognize and properly treat catatonia can lead to poor outcomes; malignant catatonia in particular can be fatal.

This topic reviews the treatment and prognosis of catatonia. The epidemiology, clinical features, assessment, underlying disorders, diagnosis, and differential diagnosis are discussed separately. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis".)

DEFINITION OF CATATONIA

Catatonia is a behavioral syndrome marked by an inability to move normally, and can occur in patients with underlying psychiatric (eg, autism spectrum disorder, bipolar disorders, psychotic disorders, and unipolar major depression) and general medical disorders. The syndrome is marked by heterogeneous signs that are observed or elicited (table 1 and table 2); the most common are immobility, rigidity, mutism, posturing, excessive motor activity, stupor, negativism, staring, and echolalia [1-3].

Subtypes of catatonia are based upon the specific nature of the movement disturbance and other associated features [1]. The three principal forms in order of incidence are:

- Retarded – Mutism, inhibited movement, posturing, rigidity, negativism, and staring
- Excited – Excessive and purposeless motor activity, restlessness, stereotypy, impulsivity, frenzy, agitation, and combativeness
- Malignant – Fever, autonomic instability (labile or elevated blood pressure, tachycardia, tachypnea, and diaphoresis), delirium, and rigidity

Additional information about the clinical features, subtypes, assessment, underlying disorders, diagnosis, and differential diagnosis of catatonia is discussed separately. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis".)

TREATMENT

Setting and management — The presence of catatonia reflects that the patient is severely ill with an underlying psychiatric or general medical disorder [4,5]. Patients are commonly hospitalized to treat the catatonic syndrome and underlying disorder, as well as to prevent and manage complications of catatonia such as aspiration pneumonia, venous thromboembolism (deep vein thrombosis and pulmonary embolism), constipation with impaction, and urinary retention [2].

Malignant catatonia in particular is life-threatening and generally warrants admission to an intensive care unit to monitor and treat [6]:

- Hyperthermia – Management of hyperthermia requires ensuring adequate airway protection, breathing, and circulation; initiation of rapid cooling; and treatment of complications. (See "Severe nonexertional hyperthermia (classic heat stroke) in adults", section on 'Management'.)
- Hypertension – Oral or parenteral medication may be necessary for severe hypertension. (See "Drugs used for the treatment of hypertensive emergencies".)
- Cardiopulmonary instability – Arrhythmias may occur from electrolyte imbalance.

For all patients with catatonia, clinicians should try to prevent and manage [7]:

- Dehydration and malnutrition – Patients who refuse to eat or drink should be monitored for input and output and may require enteral or parenteral fluids and feeding. (See

"Nutrition support in critically ill patients: An overview".)

- Deep vein thrombosis and pulmonary embolism – Deep vein thrombosis may occur in more than 25 percent of patients with catatonia; the retarded subtype of catatonia presents the highest risk [8]. Prevention and treatment of venous thromboembolism includes graduated compression stockings, intermittent pneumatic compression, and anticoagulants. (See "Prevention of venous thromboembolic disease in acutely ill hospitalized medical adults".)

- Contractures – Studies of patients with structural neurologic damage suggest that stretching and passive range of motion may prevent and treat contractures, but the results are inconsistent.

- Pressure ulcers – Pressure relief is the most important factor in preventing pressure (decubitus) ulcers and can be accomplished with proper patient positioning and appropriate use of pressure-reducing devices. Positioning of bed-bound individuals includes a regular turning and repositioning schedule (eg, every two hours), with attention to vulnerable tissue covering bony prominences such as the sacrum. (See "Epidemiology, pathogenesis, and risk assessment of pressure-induced skin and soft tissue injury" and "Prevention of pressure-induced skin and soft tissue injury" and "Clinical staging and general management of pressure-induced skin and soft tissue injury".)

- Excitement and impulsivity – Catatonic excitement and impulsivity are most safely treated with a benzodiazepine such as lorazepam, although seclusion and physical restraints are occasionally required as well. Antipsychotic drugs should be avoided. (See 'Benzodiazepine safety and administration' below and "Assessment and emergency management of the acutely agitated or violent adult", section on 'Physical restraints'.)

Underlying disorder — Management of catatonia includes treating the underlying cause as soon as it is identified, which may improve outcomes [9]. On acute inpatient psychiatric units, catatonia is most likely to occur in bipolar disorder with psychotic features and psychotic depression [10-13]. Catatonia is also associated with psychotic disorders (eg, schizophrenia) and autism spectrum disorder [5]. Many general medical conditions can progress to catatonia, including infectious, metabolic, and neurologic disorders [1,5,14]. Treatment of the general medical condition may need to be prioritized over catatonia. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis", section on 'Underlying disorders'.)

Avoid dopamine blocking drugs — Clinicians should try to avoid antipsychotics and other dopamine blocking drugs (eg, antiemetic agents) in patients with catatonia, including patients who are psychotic, impulsive, or aggressive [1]. First-generation antipsychotics do not appear to

provide any benefit for treating catatonia [15]. Although there are reports that second-generation antipsychotics may treat catatonia [2,16-19], all antipsychotics can precipitate and worsen catatonia [3,11,20]. In addition, treating catatonia with an antipsychotic is a risk factor for the neuroleptic malignant syndrome (NMS) [12,21-25]; the risk may be particularly elevated in patients who are dehydrated, receive the antipsychotic parenterally or at rapidly escalating doses, or have a prior history of catatonia [26]. Antipsychotics are contraindicated in malignant catatonia. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis", section on 'Malignant catatonia'.)

After catatonia has resolved and the patient is autonomically stable, eating and drinking normally, and moving as expected, clinicians may consider resuming an antipsychotic drug to treat an underlying psychotic disorder [12]. However, reintroducing antipsychotics should be done cautiously, with patients examined regularly for autonomic instability and recurrence of catatonic signs. If a benzodiazepine resolved the catatonic episode, it should be maintained during treatment with an antipsychotic [13]. Although high-potency, first-generation antipsychotics carry the highest risk of NMS, all second-generation antipsychotics can also cause NMS [24,27]; one case report described NMS in a patient who was treated with low-dose clozapine soon after recovering from catatonia [28].

NMS is discussed separately. (See "Neuroleptic malignant syndrome".)

Treatment algorithm — First-line treatment for catatonia is a benzodiazepine or electroconvulsive therapy (ECT), depending upon the subtype of catatonia, clinical urgency, and availability of treatments (algorithm 1) [1,15,29-33]:

- For patients with malignant catatonia, we recommend a benzodiazepine plus immediate preparation to administer ECT as soon as possible. If the benzodiazepine provides a substantive response during the first 24 to 48 hours, it can be continued in lieu of ECT.
- For patients with nonmalignant catatonia, whether the behavioral phenotype (motor disturbance) is retarded or excited, we recommend treatment with a benzodiazepine (lorazepam is used most often).

The goal of treatment is full remission.

Few randomized trials have evaluated benzodiazepines [34] or ECT [35] for acute catatonia, and these are limited to patients with nonaffective disorders. Multiple prospective open-label studies, cases series, and retrospective studies suggest that benzodiazepines alone, ECT alone, or benzodiazepines followed by ECT, lead to recovery in approximately 60 to 80 percent of patients [1,15,26,36-39]. Treatment guidelines from the American Psychiatric Association,

United Kingdom National Institute for Health and Clinical Excellence, and World Federation of Societies of Biological Psychiatry recommend treating catatonia with either a benzodiazepine or ECT, depending upon the clinical urgency [29-33].

Multiple reviews of open-label studies, case series, and case reports have found that treatment of catatonia is the same regardless of the underlying disorder [14,39,40].

In children and adolescents, the approach to treatment is the same. In a prospective observational study of youth (n = 66, ages 9 to 19 years) who were hospitalized for catatonia, 51 patients received benzodiazepines, which were effective in 65 percent of cases [40]. The benzodiazepine used most often was lorazepam (mean dose 5 mg per day); the large majority received concomitant medications such as antipsychotics. A course of bilateral ECT was administered as first-line treatment in three patients, including two with malignant catatonia, and as second-line treatment in eight other patients.

Studies suggest that catatonia may respond to the combination of benzodiazepines plus ECT [41]. Although this is not our standard practice, when the combination is employed, an agent such as flumazenil is administered prior to ECT in order to reverse the anticonvulsant properties of benzodiazepines. (See "Overview of electroconvulsive therapy (ECT) for adults", section on 'Psychotropic drugs'.)

Malignant catatonia — ECT is first-line treatment for patients with malignant catatonia (algorithm 1) [1,15,29-33]:

We recommend that clinicians concurrently start a benzodiazepine and the process of obtaining informed consent and medical consultation for ECT. If the patient does not measurably respond to a benzodiazepine within the first day or two, ECT should commence and the benzodiazepine should be discontinued. Reviews of case reports have found that mortality for progressive malignant catatonia increases if ECT does not begin within five days of symptom onset [26,42]. Another review of case reports found that in patients with malignant catatonia, response to ECT occurred in 9 of 11 patients (89 percent), whereas response to a benzodiazepine occurred in 2 of 5 patients (40 percent) [15].

For malignant catatonia that does not respond fully to initial treatment with ECT, we suggest continuing ECT until full remission is achieved. If improvement does not occur or plateaus at partial remission, we recommend continuing ECT and restarting the same benzodiazepine (eg, lorazepam) that was used while preparations were made to initiate ECT. If there is no further incremental improvement after additional ECT (eg, three more treatments), clinicians should evaluate the quality of the ECT (eg, electrode placement and stimulus) and re-evaluate the patient to determine whether the diagnosis is malignant catatonia. If ECT has been

administered properly and the diagnosis of malignant catatonia is confirmed, we suggest that treatment focus upon the underlying disorder (see 'Underlying disorder' above). As an example:

- Catatonia may be due to the neuroleptic malignant syndrome, which occurred in the context of administering a depot neuroleptic. Treatment consists of supportive care and watchful waiting while the neuroleptic is metabolized.
- Alternatively, catatonia may be secondary to mania; aggressive treatment of the manic syndrome should be pursued.

The safety and administration of benzodiazepines and ECT are discussed elsewhere in this topic. (See 'Benzodiazepine safety and administration' below and 'Electroconvulsive therapy safety and administration' below.)

Nonmalignant catatonia — Based upon prospective open-label studies and case series, we recommend initial treatment with a benzodiazepine for patients with nonmalignant catatonia, whether the behavioral phenotype (motor disturbance) is retarded or excited (algorithm 1) [1,15,29-33]:

Lorazepam has been studied most frequently [1,12,15,36,43,44], but case reports also describe successful treatment with diazepam, clonazepam, clorazepate, midazolam, and alprazolam [45-54]. In a review of case reports of 104 catatonic episodes that were treated with benzodiazepine monotherapy, 70 percent remitted; among the 72 episodes treated with lorazepam, 79 percent remitted [15]. Other reviews estimate that 60 to 80 percent of patients with catatonia respond to lorazepam monotherapy [3,45,55]. Although amobarbital was significantly more effective than placebo in a randomized trial [56], most authorities consider benzodiazepines as first-line pharmacotherapy because they are generally effective and safer than barbiturates [1-3]. In addition, benzodiazepines have been studied more often, are familiar to clinicians, and an antagonist (flumazenil) is available. (See 'Benzodiazepine safety and administration' below.)

Clinical factors may be associated with response to a benzodiazepine. Successful benzodiazepine treatment may be more likely in patients with a significant reduction of catatonic signs after the first dose of lorazepam or other benzodiazepine (positive lorazepam challenge test) [42]. Acutely catatonic patients with an underlying bipolar or depressive disorder may respond more favorably to a benzodiazepine than schizophrenic patients [13,57]. In addition, benzodiazepines at low doses do not appear to benefit chronic catatonia in schizophrenic patients. A randomized trial compared adjunctive lorazepam with placebo for treating slow-onset, long-standing (≥4 years) catatonic signs in severely disabled and treatment-resistant chronic schizophrenic patients; lorazepam 6 mg daily provided no benefit [34]. It is not clear whether a longer duration of catatonia prior to treatment is associated with a poorer

response to treatment, due to contradictory study results [13,36]. Age, sex, and the number and pattern of catatonic signs do not appear to be associated with response to a benzodiazepine [3,11,26,36]. The lorazepam challenge test is discussed separately. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis", section on 'Lorazepam challenge'.)

Based upon clinical experience, retarded or excited catatonia generally responds to a benzodiazepine within one week. For patients who do not respond to a benzodiazepine within one week, ECT is the treatment of choice [1,3,26,36]. In addition, if the underlying cause of catatonia is a bipolar or depressive disorder, or for patients requiring a rapid treatment response, ECT is the most effective treatment option. Evidence supporting the use of ECT includes a small, three-week trial that enrolled inpatients (n = 14) with nonaffective catatonia who did not respond to lorazepam (6 to 8 mg/day) within five days; patients were randomly assigned to real ECT (bilateral) plus pill placebo or to sham ECT plus risperidone (4 to 6 mg/day) [35]. Improvement of catatonia was greater with real ECT than risperidone.

Based upon open-label studies, case series, and retrospective studies, it is estimated that approximately 60 percent or more of catatonic patients achieve remission with ECT, including patients unresponsive to a benzodiazepine [3,29,36,37,43,58-60]. As an example, a review of case reports of 55 catatonic episodes that were treated with ECT alone found that 85 percent remitted [15]. A subsequent chart review of 27 catatonic patients treated with ECT found that 59 percent improved [37]. For patients with a bipolar or depressive disorder or acute psychosis, ECT can relieve both the catatonic syndrome and the underlying psychopathology [3,26]. (See 'Electroconvulsive therapy safety and administration' below.)

There are no established predictors of response to ECT for patients with catatonia [2]. However, acutely catatonic patients with an underlying bipolar or depressive disorder may respond more favorably to ECT than schizophrenic patients [57], and ECT does not appear to benefit chronic catatonia in schizophrenic patients [61].

For retarded or excited catatonia that does not respond fully to initial treatment with a benzodiazepine and subsequent treatment with ECT, we suggest continuing ECT and restarting the same benzodiazepine (eg, lorazepam) that was used initially. If there is no further incremental improvement after additional ECT (eg, three more treatments), clinicians should evaluate the quality of the ECT (eg, electrode placement and stimulus) and re-evaluate the patient to determine whether the diagnosis is retarded or excited catatonia. If ECT has been administered properly and the diagnosis of catatonia is confirmed, we suggest that treatment focus upon the underlying disorder (see 'Underlying disorder' above). In addition, it is reasonable to use other treatments that are described below. (See 'Other treatments' below.)

Benzodiazepine safety and administration — Benzodiazepines are generally safe and well tolerated in this setting. At doses used for treating catatonia, benzodiazepines are not associated with respiratory depression in otherwise healthy adults. However, clinicians should be cognizant of concomitant drugs (eg, opioids) that can cause sedation or respiratory depression. In addition, benzodiazepines cause varying degrees of motor incoordination and increase the risk of falls [12].

Benzodiazepines can be administered intravenously, intramuscularly, or orally (lorazepam is available in all three formulations) [3,36]. Intravenous administration is preferred to assure adherence and rapid, complete absorption (intravenous access also permits administration of fluids for dehydration). Intravenous benzodiazepines should be injected or infused slowly. As patients improve, they should be switched to oral medication.

Lorazepam has been studied most often, and is typically initiated at 1 to 2 mg three times per day. For patients who are already receiving lorazepam for another indication when they present with catatonia, the starting dose of lorazepam for catatonia (eg, 1 mg three times per day) is added to the existing dose of lorazepam (eg, 1 mg each night for insomnia). Close observation for a clinical response can substantiate the diagnosis of catatonia. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis", section on 'Lorazepam challenge'.)

Subsequently, the dose is increased by 3 mg per day every one to two days, depending upon patient response, tolerability, and clinical urgency. A dose of 6 to 21 mg daily is effective for most patients, but a dose of 30 mg per day is occasionally necessary [1]. For patients with excited catatonia, lorazepam 1 to 2 mg is given at more frequent intervals until the patient is calm but awake.

A more cautious approach is suggested for patients at risk of cardiorespiratory compromise or oversedation, including patients with:

- Cardiovascular or respiratory disease
- Older age
- Obesity
- Volume depletion
- Prescriptions for opioid analgesics

For patients with these risk factors, the initial dose may be reduced to 0.5 mg three times per day and closer monitoring provided [12,43].

The duration of treatment required to achieve remission of catatonia with a benzodiazepine is typically 4 to 10 days [42]. The benzodiazepine is usually continued at the effective dose for

three to six months to maintain recovery and is then slowly tapered and discontinued, although longer maintenance treatment may be necessary [62].

Drug information topics are available for specific benzodiazepines.

Electroconvulsive therapy safety and administration — ECT is generally safe, even in patients whose general medical status is compromised [63], as well as patients who are pregnant [64] or older (eg, ≥65 years) [65]. However, the success of ECT depends upon an appropriate pre-ECT evaluation, the goals of which are to optimize treatment efficacy and minimize the risk of cognitive and other side effects associated with ECT. ECT is typically administered with the same technique used for other indications. (See "Medical evaluation for electroconvulsive therapy" and "Technique for performing electroconvulsive therapy (ECT) in adults".)

There are no absolute contraindications to ECT [66-70]. Underlying general medical conditions may increase the risk of adverse effects of ECT or general anesthesia, but modern ECT technique and preprocedure consultation to optimize the patient's general medical status reduce these risks. As an example, catatonic patients with motor immobility and muscle damage are at increased risk for transient hyperkalemia associated with the muscle relaxant succinylcholine [2,14]. This increased risk is eliminated by using a nondepolarizing muscle relaxant (eg, rocuronium) [71].

Electrode placement and other aspects of ECT technique for treating catatonia have not been standardized [14]. However, bitemporal electrode placement and brief pulse current are generally preferred [1]. ECT is generally given three times per week on alternating days. However, for patients with malignant catatonia, we suggest daily treatments until the patient is physiologically stable, which often occurs within two to five treatments [1,72]. At least six treatments are given regardless of the catatonia subtype to reduce the risk of sudden relapse. Most patients receiving ECT regardless of the indication remit with 6 to 12 treatments, but some patients may require 20 or more [63]. ECT is usually terminated after the acute catatonic episode has remitted, but one case report described maintenance ECT for a patient with recurrent catatonia [73]. Additional information about ECT is discussed separately. (See "Overview of electroconvulsive therapy (ECT) for adults" and "Technique for performing electroconvulsive therapy (ECT) in adults".)

Case reports describe catatonic patients who responded to ECT plus lorazepam [69,70]. The decision to continue a benzodiazepine during ECT is determined by the patient's initial response to the medication and the modifications in ECT technique that are required. For patients with a partial but incomplete response to lorazepam, the drug may be continued during ECT to

maintain the drug's therapeutic benefit. However, the benzodiazepine should be discontinued if it interferes with ECT (increases seizure threshold and shortens seizure duration) despite adjustments in the ECT technique. (See "Overview of electroconvulsive therapy (ECT) for adults", section on 'Concurrent medications'.)

Other treatments — Alternative treatments may be available for patients with catatonia who do not respond to benzodiazepines and decline ECT or do not respond to ECT or have access to it [3]. Case reports describe other treatments that were added to an existing pharmacotherapy regimen and may possibly be beneficial. These other treatments include carbamazepine [74], topiramate [75], valproate [76,77], zolpidem [3,78,79], memantine [80-83], and bromocriptine [84]. Amantadine has also been used, but has dopamine agonist activity that can potentially worsen an underlying psychosis [83]. Additional case reports describe treatment of catatonia with repeated transcranial magnetic stimulation [14].

LONG-TERM PROGNOSIS

Although the long-term outcome of catatonia has not been rigorously studied, catatonia appears to have a generally favorable prognosis, especially the retarded and excited subtypes [3,85]. Long-term prognosis appears to be linked to the nature and severity of the underlying psychiatric or general medical disorder [2,26]. Retarded or excited catatonia in patients with an underlying bipolar or depressive disorder or toxic-metabolic disorder usually resolves with treatment of the catatonic syndrome plus the underlying condition [26]. However, catatonia may persist for years, particularly in patients with schizophrenia [34]. In addition, patients with malignant catatonia may be left with permanent morbidity (eg, cognitive deficits, apathy syndromes, and limb strictures), and death rates of up to 20 percent have been reported [42].

Case reports describe recurrent catatonic episodes [15,73]. One case series of five patients reported that the mean interval between consecutive episodes was 11 months (range 5 to 20 months) [86]. The motor signs were generally consistent across each patient's two episodes. For cases with complete information, the same treatment worked in the two episodes.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Depressive disorders".)

SUMMARY AND RECOMMENDATIONS

- **Definition of catatonia** – Catatonia is a behavioral syndrome marked by an inability to move normally despite full physical capacity to do so. The syndrome is associated with many psychiatric, neurologic, and general medical disorders. Signs of catatonia are listed in the tables (table 1 and table 2). The three primary subtypes of catatonia are retarded, excited, and malignant. (See 'Definition of catatonia' above and "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis".)

- **Treatment setting** – Treatment of acute catatonia generally occurs in hospital settings where the patient's general medical health can be monitored and optimized. Malignant catatonia in particular is life-threatening and generally warrants admission to an intensive care unit. (See 'Setting and management' above.)

- **Treating the underlying disorder** – Concurrently treating the underlying psychiatric or general medical disorder along with the catatonia may improve outcomes. Clinicians should avoid using dopamine blocking drugs, even if patients are psychotic, impulsive, or aggressive. Treating catatonia with an antipsychotic is a risk factor for the neuroleptic malignant syndrome (NMS). Antipsychotics are contraindicated in malignant catatonia. (See 'Underlying disorder' above and 'Avoid dopamine blocking drugs' above.)

- **Treating malignant catatonia** – Mortality in malignant catatonia may increase if electroconvulsive therapy (ECT) does not begin within five days of symptom onset. For patients with malignant catatonia, we recommend ECT rather than a benzodiazepine (algorithm 1) (**Grade 1C**). A benzodiazepine should be administered during preparations for ECT; if malignant catatonia improves significantly with the benzodiazepine during the first 24 to 48 hours, it can be continued in lieu of ECT. (See 'Treatment algorithm' above and 'Malignant catatonia' above.)

- **Treating nonmalignant catatonia** – For patients with nonmalignant catatonia, whether the behavioral phenotype (motor disturbance) is retarded or excited, we recommend a benzodiazepine rather than ECT (**Grade 1C**). For retarded or excited catatonia that does not respond to a benzodiazepine, we suggest ECT rather than other medications (**Grade 2C**). (See 'Treatment algorithm' above and 'Nonmalignant catatonia' above.)

- **Selecting and administering a benzodiazepine** – The benzodiazepine used most often is intravenous lorazepam 1 to 2 mg three times per day, which is increased by 3 mg per day every one to two days. A dose of 6 to 21 mg daily is effective for most patients, but a dose of 30 mg per day is occasionally necessary. The benzodiazepine is usually continued orally at the effective dose for three to six months and then tapered and discontinued. Following remission of catatonia, the benzodiazepine should be continued if an antipsychotic drug is

used to treat the underlying disorder. (See 'Benzodiazepine safety and administration' above.)

- **Administering ECT** – There are no absolute contraindications to ECT. For catatonic patients with motor immobility and muscle damage, a nondepolarizing muscle relaxant is used to eliminate the risk of transient hyperkalemia associated with the use of the succinylcholine. ECT is generally given three times per week on alternating days, but malignant catatonia may initially require daily treatments. ECT is typically administered at least six times with bilateral electrode placement and brief pulse current. (See 'Electroconvulsive therapy safety and administration' above.)

- **Long-term prognosis** – Retarded and excited catatonia both appear to have a generally favorable prognosis, especially in patients with an underlying bipolar or depressive disorder or toxic-metabolic disorder. By contrast, malignant catatonia may result in permanent morbidity, and death rates of up to 20 percent have been reported. (See 'Long-term prognosis' above.)

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