

Atrial infarction: Diagnosis and management

Eliot J. Lazar, MD, Jeffrey Goldberger, MD, Harry Peled, MD,
Michael Sherman, MD, and William H. Frishman, MD. *Bronx, N.Y.*

Atrial infarction has to date been a relatively understudied entity. The reasons for this include difficulty in accurate diagnosis, lack of understanding of its clinical relevance, and the overshadowing implications of the oft accompanying ventricular infarction. In this review, we will discuss the incidence, clinical characteristics, and currently available diagnostic criteria for atrial infarction. More importantly, we will attempt to demonstrate that infarction of the atria represents a distinct clinical entity apart from ventricular infarction which, when recognized, may lead to significant modifications in therapy.

HISTORY AND INCIDENCE

The first case of atrial infarction was described by Clerc and Levy in 1925.¹ A 60-year-old man presented in congestive heart failure, and on postmortem examination, a hemorrhagic infarct was noted in the right auricle. The first electrocardiographic demonstration of atrial infarction was in 1937²; however, the diagnosis was made retrospectively after postmortem examination. The first antemortem diagnosis of atrial infarction, on the basis of P-Ta segment changes in the presence of complete heart block on a standard surface electrocardiogram, was in 1948.³ (Ta represents the atrial T wave or repolarization, which normally is hidden in the QRS complex). In 1938, Bean⁴ reported a pathologic series of 287 cases of myocardial infarction that included two cases of atrial infarction, representing an 0.7% incidence. In 1942, Cushing et al.⁵ reported the largest series of autopsy-proven atrial infarctions, which included 31 out of 182 cases of fatal myocardial infarction, an incidence of 17%. The highest reported incidence by autopsy study is 42%.⁶ This wide variation in reported incidence⁴⁻⁸ of atrial infarction may be a

reflection of whether or not the atria are specifically examined for areas of necrosis.⁵

ANATOMY AND PATHOLOGY

The atria, like the ventricles, are supplied by branches of the coronary arteries. In most cases there are a number of branches from the right coronary artery.^{5,10} The main branch feeds the anterior wall of the right atrium, as well as the auricle. It then penetrates the septum to reach the posterior wall, where it wraps around the superior vena cava, resulting in a plexus. At times this first branch originates from the left coronary artery, encircles the base of the left auricle, and ascends to the left atrium, to reach the plexus surrounding the superior vena cava. In either case, the artery of the sinoatrial node arises from this plexus. The next branch from the right coronary artery is somewhat variable and supplies the anterosuperior aspect of the left atrium.⁵ Alternatively there may be branches from the left coronary artery.¹⁰

As suggested earlier, atrial infarctions are often missed under routine pathologic examination unless specifically looked for. In the study of Cushing et al.,⁵ on autopsy, routine blocks were taken from the region of the sinoatrial node, both auricles, and the lateral wall. Mural thrombi increased the examiner's suspicion of atrial involvement and hence sections were also obtained from the juxtaposed areas. These investigators found that of the total of 31 cases, 27 infarctions occurred in the right atrium and five occurred in the left atrium. In 21 of the 27 right-sided infarcts, the auricle was involved, while three of five left-sided infarcts showed auricular involvement. Only 2 of the 31 cases involved the sinoatrial node. Interestingly, 6 of the 31 cases displayed atrial involvement without ventricular involvement.

The area of atrial infarction is usually located near the atrioventricular groove. Since the atria are so thin, when they are involved the process is usually transmural.⁹ Microscopically, infarction of the atria is similar to that seen in the ventricle, with throm-

From the Department of Medicine, Division of Cardiology, The Albert Einstein College of Medicine.

Received for publication Apr. 25, 1988; accepted June 15, 1988.

Reprint requests: Eliot J. Lazar, MD, Jack D. Weiler Hospital of the Albert Einstein College of Medicine, 1825 Eastchester Rd., Bronx, NY 10461.

bosis being most commonly associated with massive infarction.

ETIOLOGY

The vast majority of atrial infarctions are felt to be due to arteriosclerotic heart disease.¹⁰ However, Howard et al.¹¹ in 1970 reported on seven cases of atrial infarction in an autopsy series, of which four had chronic obstructive pulmonary disease (COPD) with cor pulmonale and essentially normal coronary arteries. They suggested that a state of relative hypoxia from pulmonary disease and increased pressure and volume loads on the atria may have been contributory. Other conditions in which infarction of atrial muscle or conduction tissue, i.e., sinus node, have been reported include primary pulmonary hypertension,¹² muscular dystrophy,¹³ and Friedreich's ataxia.¹⁴

CLINICAL CHARACTERISTICS

It has been felt that making the diagnosis of atrial infarction is of little clinical importance,³ as its prognosis is largely dependent on the prognosis of the accompanying ventricular infarction rather than upon the atrial infarction itself. We will attempt to demonstrate that atrial infarction may indeed be of clinical importance.

The majority of atrial infarctions involve the right side.^{3,15} Gardin and Singer¹⁶ reviewed several larger series and found the right atrium involved in 81% to 98%, the left atrium involved in 2% to 19%, and biatrial involvement in 19% to 24%. The clinical characteristics of atrial infarction can be divided into two groups: (1) those in which the effects of ventricular infarction predominate and (2) those due directly to atrial involvement. As one might suspect, this distinction is often difficult to make.

A variety of complications have been associated with atrial infarction (Table I). These include arrhythmia, rupture, loss of atrial "kick," and thromboembolic phenomena.^{5,16,17} Arrhythmias are quite common in the setting of atrial infarction and include paroxysmal atrial fibrillation, wandering atrial pacemaker, and atrial premature contractions, with runs of atrial tachycardia.¹⁸ Characteristic of these arrhythmias are their sudden onset and disappearance.⁷ The reported incidence ranges from 61% to 74%,¹⁰ as opposed to an overall incidence of 8%⁵ in ventricular infarction alone. Given the deleterious effects of these tachyarrhythmias in the setting of myocardial infarction, it would be useful to predict their occurrence and hence effect early intervention. It is possible that type IA antiarrhythmic agents

Table I. Complications of atrial infarction

Rhythm disturbances
Supraventricular tachycardia
Atrial fibrillation
Wandering atrial pacemaker
Sinus tachycardia +/- APCs
Sinus arrest
Thromboembolic phenomena
Pulmonary emboli
Systemic emboli
Atrial rupture
Hemodynamic consequences
Loss of atrial "kick"

APCs = atrial premature contractions.

may be useful prophylactic agents, particularly since lidocaine has little effect on supraventricular arrhythmias.¹⁹ Alternatively, verapamil, digoxin, or a beta blocker might be recommended to slow the ventricular rate if these arrhythmias do occur. Sinus arrest has also been reported²⁰ with infarction in the region of the sinoatrial node. To date there have been no reported cases of ventricular dysrhythmias associated with atrial infarction alone.

Another common complication of atrial infarction is mural thrombus with embolism. Cushing et al.⁵ reported an 84% incidence of thrombi in cases of atrial infarction. Pulmonary emboli were seen in 24% of patients in another series.²¹ Since the majority of atrial infarctions occur in the right atrium,⁸ one would expect pulmonary emboli to be more common than those of the systemic circulation. However, a case of an embolus from the left atrium causing total obstruction of both iliac arteries has been reported.²² Given this high rate of embolism, it is intriguing to hypothesize that a subset of patients with ventricular infarction and concurrent, unrecognized atrial infarction may account for a significant portion of the pulmonary embolic phenomena observed with ventricular infarction. Confirmation of this hypothesis may provide cogent reasons for routinely anticoagulating those patients with demonstrable atrial infarction.

Rupture of the atrium is another complication of atrial infarction. The incidence of rupture in proven cases of atrial infarction has been reported to be as high as 4.5%. In the 80 cases of atrial rupture reported by Kohn et al.,¹⁷ 10 were attributable to atrial infarction. The clinical presentation in these cases was similar to that seen with ventricular rupture. Death always occurred with atrial rupture, usually within 24 hours, with the longest survival

through 9 weeks. However, 15% of patients with atrial rupture survived longer than 24 hours compared to 2% of patients with ventricular rupture. Signs of cardiac tamponade may develop in patients who survive the initial event. Thus if the diagnosis of atrial infarction is suspected or established and signs of cardiac tamponade develop, early intervention may be effected. In a recent case report,²³ a patient developed an atrial rupture 4 days before subsequent death from ventricular rupture. Thus atrial rupture, a severe complication of atrial infarction, went unrecognized for 4 days, once again indicating that if the diagnosis can be established, the patient can survive long enough to attempt surgical repair. Since atrial rupture is a lesion potentially correctable by surgery, the possibility of atrial infarction and its resultant sequelae must be considered, particularly in the face of hemodynamic compromise. Interestingly, the above patient likely developed atrial rupture during an unsuccessful attempt to place an electrode through the right subclavian vein. As most atrial infarctions are right-sided,^{5, 10, 24, 25} central catheter placement may be relatively contraindicated in patients with atrial infarctions.

Several studies²⁶⁻³¹ have shown that atrial contraction contributes significantly to cardiac output. This is particularly important in diseased hearts.^{26, 27} In atrial infarction, a presumed reduction in atrial "kick" due to ischemia or necrosis might have significant hemodynamic consequences. The importance of atrial "kick" is revealed by studies that showed decreased cardiac output with atrial fibrillation^{28, 29} or any supraventricular arrhythmia.²⁹ The increase in cardiac output seen with atrioventricular sequential pacing, as opposed to ventricular pacing,^{30, 31} provides further evidence of the importance of the atrial contraction. Therefore it is possible that patients with atrial infarction may be more likely to have difficulty maintaining their ventricular filling pressure. Analogous to patients with right ventricular infarction, patients with atrial infarction might benefit from aggressive loading of fluid (while at the same time showing evidence of right-sided volume overload).

An additional reason to search for evidence of atrial infarction is to suggest the diagnosis of ventricular infarction that could not otherwise be made.^{16, 18} A likely situation in which this can occur is in patients with left bundle branch block. In fact, Liu et al.¹⁸ suggest that all patients with evidence of atrial infarction alone should be managed as if they had ventricular infarction, because there may be ventricular involvement that is not manifest on the electrocardiogram (ECG).

DIAGNOSIS

Electrocardiography has been the primary instrument for antemortem diagnosis. As the clinical significance of atrial infarction is not yet fully established, attempts to establish rigid ECG criteria for its diagnosis have been minimal. Compounding this problem is the fact that any given atrial infarction may not be manifest on routine ECG recordings. Because of the low voltage generated by the atria, their thin walls, and the larger overshadowing ventricular depolarization, ECG changes associated with atrial infarction may be absent or missed. However, various electrical criteria for the diagnosis of atrial infarction have been proposed. These include changes in the PTa segment, changes in P wave morphology, and the occurrence of supraventricular arrhythmias.^{7, 18, 32, 34, 40} On scrutiny of these criteria, it becomes evident that they are neither specific nor sensitive for the diagnosis of atrial infarction.^{16, 24, 32, 33}

Changes in the PTa segment are difficult to interpret, as they may occur in normal people as well. Shipley and Halloran³⁵ reported a series of 200 "normal" ECGs in which 55% showed depression of the PTa segment in lead I and 1% showed an elevation. In no case was the depression greater than 0.8 mm or the elevation greater than 0.4 mm. Larsen and Skulason³⁶ also reported a series of 100 normal people. On examination of their patients' ECGs, they found PTa segment depression 14 times in lead I, 54 times in lead II, and 21 times in lead III. Elevation of the PTa segment was found 12 times in lead III and not at all in leads I or II. The maximum deviation in either direction was 0.5 mm. Conversely Burch⁹ reported that "P-R segment depression of a fraction of a millimeter or more" was associated with atrial infarction in 100% of the cases from a long-term autopsy study. Deviations of the PTa segment in atrial infarction need to be studied to find a reasonably sensitive and specific cut-off point. Another problem with the use of PTa segment deviation is its occurrence in other conditions. These include pericarditis³⁷ and atrial overload.³⁸ However, when the PTa segment shifts in atrial infarction, Burch⁹ proposes that it behaves as the ST segment does with ventricular infarction, except that it shifts less frequently and rarely elevates during infarction. He also notes⁹ that PTa depression may occur during episodes of angina pectoris and disappear when the anginal episode subsides; but with infarction, the PTa segment slowly returns to baseline as the infarct heals. Only in rare cases does the PTa segment never return to baseline. The ischemic nature of PTa segment changes may be confirmed by evolution of the tracing over time.⁷ Cushing et al.⁵

reported 31 cases of atrial infarction. Of the 23 ECGs obtained, five showed PTa segment depression. However, these investigators felt this sign was of doubtful significance because of its occurrence in normal individuals, as noted above.^{35,36} PTa segment changes, when they occur, should theoretically depend on the location of the infarct, analogous to the ST segment deviations in ventricular infarctions. For example, injury of the subepicardial myocardium of the posterior basal wall should show positive deviation in lead III, usually positive deviation in lead II, and negative deviation in lead I. Anterior or anterolateral lesions should show depression in lead III and elevation in lead I.

The P wave itself can undergo a variety of alterations. It can be enlarged and flattened, inverted, bifid or biphasic. These changes occur frequently but are nonspecific. Supraventricular arrhythmias also constitute an important diagnostic element. Cushing et al.⁵ found that 17 out of 23 patients with atrial infarctions had supraventricular arrhythmias—atrial fibrillation in nine cases, atrial premature complexes in four cases, atrial flutter in two cases, sinus arrest in one case, and wandering pacemaker in one case. In addition, in six patients who had atrial infarction without evidence of any ventricular involvement, two showed atrial fibrillation, one showed atrial flutter, and one showed low QRS voltage. Overall, in the study by Cushing et al.,⁵ which included 31 cases of atrial infarction in 182 cases of myocardial infarction (again, only 23 ECGs were obtained), abnormalities in the atrial complex were present in 74% (17 of 23) of cases (of atrial infarction), contrasted with a 9% (8 of 91) incidence of abnormalities in cases of ventricular infarction only. Various authors^{24,39} also describe an atrial Q wave in analogy to ventricular Q waves. However, the diagnostic value of atrial Q waves as an ECG sign is contested, and its real significance is not yet entirely established.⁷

Practically, how does one make a diagnosis of atrial infarction by ECG means? Liu et al.¹⁸ reported both major and minor ECG criteria for its diagnosis (Table II). The major criteria include: PTa segment elevation greater than 0.5 mm in leads V₅ and V₆ with reciprocal PTa segment depression in V₁ and V₂; or PTa segment elevation greater than 0.5 mm in lead I with reciprocal depression in leads II or III; or PTa segment depression greater than 1.5 mm in the precordial leads and 1.2 mm in leads I, II, and III in association with any form of atrial arrhythmia. The minor criteria include abnormal P waves—M-shaped, W-shaped, irregular, or notched. Depression of the PTa segment of small amplitude without reciprocal elevation in other leads cannot by itself be

Table II. Electrocardiographic diagnostic criteria*

Major criteria

1. PTa segment elevation >0.5 mm in leads V₅ and V₆ with reciprocal PTa segment depression in leads V₁ and V₂
2. PTa segment elevation >0.5 mm in lead I with reciprocal depression in leads II and III
3. PTa segment depression >1.5 mm in precordial leads and 1.2 mm in leads I, II, and III in association with any atrial arrhythmias

Minor criteria

1. Abnormal P waves: M-shaped, W-shaped, irregular, or notched

*As proposed by Liu.

regarded as positive evidence of atrial infarction. More recently Mayuga and Singer⁴⁰ suggested adding the following criteria to those stated by Liu: "(1) Evolutionary changes in P-wave contour and in the J(a)-point and P-R segment in serial tracings and (2) concurrent appearance of atrial arrhythmias, changes in P-wave contour and P-R segment changes." They further point out that in the presence of preexisting P-wave abnormalities, caution must be exercised in interpreting PR segment criteria. Perhaps the use of specialized electrical recordings, such as high-gain surface "atriograms,"²³ intraatrial recordings (especially in a patient who is to undergo right-sided catheterization anyway), or Lewis leads will be even more helpful in identifying cases of atrial infarction. In the meantime, the clinician must use the available criteria to establish this often overlooked diagnosis. Other noninvasive means of diagnosing atrial infarction have not been extensively studied, although case reports have been published. Gordon et al.⁴¹ described a case of right atrial infarction complicating an acute inferior and right ventricular myocardial infarction that was diagnosed by cardiac gated blood pool scan. It would have been interesting in this case, as pointed out by Spodick,⁴² to have had accompanying ECG data while the patient was in normal sinus rhythm at the time of the scan.

Echocardiography has thus far shown only limited utility in the setting of atrial infarction. This is probably due in part to the limited ability to visualize the atria, particularly the right atrium, with the standard imaging planes. Esophageal echocardiography, which allows better visualization of the atria, may provide a new modality for making this diagnosis. Sasaki et al.⁴³ reported a case of right atrial infarction in the setting of an acute inferoposterior myocardial infarction 1 month earlier. They suggested that esophageal echocardiography was indicated to evaluate atrial wall motion when this diagnosis

was suspected. Further studies are needed to support this view.

In conclusion, atrial infarction is a distinct, well-described, yet underdiagnosed clinical entity. Its significance to the clinician has to date been only partially explored. Further investigative work is still needed to fully elucidate the role of atrial infarction in the etiology of peri- and postinfarction complications. Perhaps a subset of patients can eventually be delineated who would benefit from variations in routine post-myocardial infarction management based on atrial involvement. We anxiously await additional data in this regard.

SUMMARY

Atrial infarction has been a relatively understudied entity. Its incidence by autopsy study has been widely variable, from 0.7% to 42%, with the largest series of 182 patients demonstrating an incidence of 17%. The right atrium is involved five times as often as the left, with the auricle the predominant site in either atria. Clinical atrial infarction may present with supraventricular arrhythmias, atrial rupture, hemodynamic compromise from loss of atrial "kick," and thromboembolic phenomena. Diagnosis currently is made in an appropriate clinical setting with characteristic PR interval changes. Other noninvasive techniques have shown only limited diagnostic utility, but esophageal echocardiography may prove to be a useful technique in this setting.

REFERENCES

- Clerc A, Levy R. Infarctus auriculaire: tachyarrhythmie terminale. *Bull Mem Soc Med Hop Paris* 1925;41:1603-7.
- Langendorf R. Elektrokardiogram bei Vorhof-Infarkt. *Acta Med Scand* 1939;100:136-49.
- Hellerstein HK. Atrial infarction with diagnostic electrocardiographic findings. *AM HEART J* 1948;36:422-30.
- Bean WB. Infarction of the heart. *Ann Intern Med* 1938;12:71-94.
- Cushing EH, Feil HS, Stanton EJ, et al. Infarction of the cardiac auricles (atria): clinical, pathological and experimental studies. *Br Heart J* 1942;4:17-34.
- Wartman WB, Sanders JC. Localization of myocardial infarcts with respect to the muscle bundles of the heart. *Arch Pathol Lab Med* 1950;50:321-64.
- Van Durme JP, Bossaert L, Vermeere P, et al. L'electrocardiogramme intra-auriculaire dans le diagnostic de l'infarctus de l'oreillette. *Arch Mal Coeur* 1972;65:885-9.
- Friedberg CK. Diseases of the heart. 3rd ed. Philadelphia: W.B. Saunders Co., 1966.
- Burch GE. Of the P-R segment depression and atrial infarction. *AM HEART J* 1976;91:129-30.
- Soderstrom N. Myocardial infarction and mural thrombosis in the atria of the heart. *Acta Med Scand* 1948;217(Suppl):1-113.
- Howard JF, Leach JK, Weitzner S, et al. Atrial infarction. With chronic obstructive lung disease. *Rocky Mt Med J* 1970;67:47-51.
- James TN. On the cause of syncope and sudden death in primary pulmonary hypertension. *Ann Intern Med* 1962;56:252-64.
- James TN. Observations on the cardiovascular involvement including the cardiac conduction system in progressive muscular dystrophy. *AM HEART J* 1962;63:48-56.
- James TN. Observations on the cardiovascular involvement in Friedreich's ataxia. *AM HEART J* 1963;66:164-75.
- Flowers NC, Horan LG. Atrial infarction. *Dis Chest* 1966;49:638-40.
- Gardin JM, Singer DH. Atrial infarction: importance, diagnosis and localization. *Arch Intern Med* 1981;141:1345-8.
- Kohn RM, Harris R, Gorham LW. Atrial rupture of the heart. *Circulation* 1954;10:221-31.
- Liu CK, Greenspan G, Piccirillo RT. Atrial infarction of the heart. *Circulation* 1961;23:331-8.
- Zipes DP. Management of cardiac arrhythmias. In: Braunwald E, ed. *Heart disease: a textbook of cardiovascular medicine*. Philadelphia: W.B. Saunders Co., 1987:627-34.
- Young EW, Koenig A. Auricular infarction. *AM HEART J* 1944;28:287-94.
- Hellerstein HK, Martin JW. Incidence of thromboembolic lesions accompanying myocardial infarction. *AM HEART J* 1947;33:443-52.
- Fujiwara H, Saimyoji H, Kawai C, et al. Left atrial infarction with saddle embolism. *Jpn Heart J* 1977;18:272-6.
- Cristal N, Pewterberg I, Inbar-Yonai I. Atrial infarction leading to rupture. *Br Heart J* 1979;41:350-3.
- Freundlich J, Sereno LR. Auricular infarction. *AM HEART J* 1959;57:654-60.
- Wartman WB, Hellerstein HK. The incidence of heart disease in 2000 consecutive autopsies. *Ann Intern Med* 1948;28:41-65.
- Lassers BE, Anderfon JL, George M, et al. Hemodynamic effects of artificial pacing in complete heart block complicating acute myocardial infarction. *Circulation* 1968;38:308-23.
- Rahimtoola SH, Eshani A, Sinno MZ, et al. Left atrial transport function in myocardial infarction: Importance of its booster function. *Am J Med* 1975;59:686-94.
- Morris JJ, Entman M, North WC, et al. The changes in cardiac output with reversion of atrial fibrillation to sinus rhythm. *Circulation* 1965;31:670-8.
- McIntosh HD, Kong Y, Morris JJ. Hemodynamic effects of supraventricular arrhythmias. *Am J Med* 1964;37:712-27.
- Topol EJ, Goldschulser N, Ports TA. Hemodynamic benefit of atrial pacing in right ventricular myocardial infarction. *Ann Intern Med* 1982;96:594-7.
- Nader DA, Cerretto WJ, Vives WY. Atrial pacing in the management of right ventricular infarction. *South Med J* 1981;74:362-3.
- James T. Myocardial infarction and atrial arrhythmias. *Circulation* 1961;24:761-76.
- Dicosky C, Zimmerman H. Atrial injury. *J Electrocardiol* 1969;2:51-4.
- Meerschwan IS, Dekker E, Durrer D. Un cas d'infarctus de l'oreillette confirme par derivations endocavitaires. *Arch Mal Coeur* 1965;58:558-63.
- Shipley RA, Halloran WR. The four lead EKG in two hundred normal men and women. *AM HEART J* 1936;11:325-45.
- Larsen K, Skulason T. The normal EKG. *AM HEART J* 1941;22:625-60.
- Zimmerman HA, Bersano E, Dicosky C. The auricular electrocardiogram. Springfield, Illinois: Charles C. Thomas, 1968.
- Hahn L, Langendorf R. Morphologie des Vorhof-elektrokardiogramms rechts-und-links-hyperfunktionstypus des Vorhof-elektrokardiogramms. *Acta Med Scand* 1939;100:279-95.
- Sanders A. Experimental localized auricular necrosis: electrocardiographic study. *Am J Med Sci* 1959;198:690-4.
- Mayuga RD, Singer DH. Atrial infarction: clinical signifi-

- cance and diagnostic criteria. *Practical Cardiol* 1985;11:142-60.
41. Gordon S, Finck DR, Perera RD, et al. Atrial infarction complicating an acute inferior myocardial infarction. *Arch Intern Med* 1984;144:193.
42. Spodick DH. Diagnosing atrial infarction [Letter]. *Arch Intern Med* 1984;144:2429.
43. Sasaki T, Matsuzaki M, Anno Y, et al. Diagnosis of right atrial infarction by esophageal echocardiography. *J Cardiogr* 1982;12:595-604.

How effective is digitalis in the treatment of congestive heart failure?

Carey Kimmelstiel, MD, and Joseph R. Benotti, MD. *Worcester, Mass.*

"The use of the foxglove is getting abroad, and it is better the world should derive some instruction, however imperfect, from my experience, than the lives of men should be hazarded by its unguarded exhibition or that a medicine of so much efficacy should be condemned and rejected as dangerous and unmanageable."¹

Over 200 years have passed since the above words appeared in William Withering's classic treatise documenting his 10-year experience prescribing digitalis for the treatment of the dropsy. Digitalis preparations remained the major pharmacologic treatment for congestive heart failure (CHF) until the 1950s, when oral diuretic agents became available for clinical use. Although there is a general consensus concerning the utility of digitalis in the treatment of most forms of CHF complicated by supraventricular tachyarrhythmias,²⁻⁴ major controversy persists regarding its efficacy in heart failure patients who are in sinus rhythm.⁵⁻⁷ Some of the reasons for avoiding digitalis use in these patients include doubt concerning the drug's chronic inotropic effect,⁸ the lack of a measurable therapeutic target such as heart rate in the patient with atrial fibrillation,^{3,7} the drug's possible deleterious effect on the myocardial oxygen supply/demand ratio,^{9,10} the possibility of induced digitalis toxicity,^{8,11} and the possibility of digitalis interactions with concomitantly given medications.⁸

In this article we review the evidence that digitalis causes a sustained inotropic effect when given over a long term. The published clinical trials testing the efficacy of digitalis in patients with chronic CHF are summarized, with particular emphasis on those patients in sinus rhythm. We also review studies relating to the administration of digitalis to a group of patients exemplifying the majority of the heart failure population, those with advanced coronary artery disease. Finally, we address several associated issues relating to digitalis administration alluded to above.

DOES DIGITALIS HAVE A SUSTAINED INOTROPIC ACTION?

Digitalis-induced enhancement of myocardial contractility has been questioned by a variety of authors^{7,12-14} concern relates to the clinical significance of the augmented contractility noted in the laboratory. Digitalis augmentation of myocardial contractility has been shown in a variety of studies—in isolated muscle preparations, in intact animals and humans, as well as in normal and failing myocardium.

In 1965, Sonnenblick et al.¹⁵ at the National Heart Institute used isolated human papillary muscles to document significant increases in the development of isometric tension generated by the muscle as well as increases in the maximal velocity of shortening when the glycoside strophanthidin was added to the bath. In 1974, Carliner et al.,¹⁶ who used oral digoxin therapy in eight patients in sinus rhythm, documented a dose-related positive inotropic effect, as evidenced by a significant shortening of systolic time intervals after roughly 2 weeks of therapy.

From the Division of Cardiovascular Medicine, University of Massachusetts Medical Center.

Received for publication Apr. 25, 1988; accepted June 10, 1988.

Reprint requests: Carey Kimmelstiel, MD, Division of Cardiovascular Medicine, University of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, MA 01655.