

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format on for each person. (See attached sample). **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
Holly Ruth Middlekauff, M.D.		Associate Professor of Medicine	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Yale University, New Haven, CT	B.S. Cum Laude	1978-1982	Biochemistry
USC School of Medicine, Los Angeles, CA	M.D.	1982-1986	Medicine

A. Positions and Honors.**Positions and Employment**

1986 – 1989	Internal Medicine Resident, UCLA Medical Center
1989 – 1990	Electrophysiology Fellow, UCLA Medical Center
1990 – 1992	Cardiology Fellow, UCLA Medical Center
1991 – 1992	Chief Resident, Internal Medicine
1992	Visiting Scientist, University of Iowa Hospitals and Clinics
1992 – 1999	Assistant Professor of Medicine, Division of Cardiology, UCLA School of Medicine
1999 – Present	Associate Professor of Medicine, Division of Cardiology, UCLA School of Medicine

Honors

1985	Alpha Omega Alpha Honor Medical Society, Vice President
1991	American College of Cardiology Travel Award
1992 – 1993	Mark C. Lidwill Traveling Fellowship Award
1994	Laverna Titus Young Investigator Award, American Heart Association
1997	Development Partners Junior Faculty Award, SmithKline Beecham
1999 – 2000	Teacher of the Year, UCLA Medical Center

B. Selected peer-reviewed publications (in chronological order).

1. **Middlekauff HR**, Stevenson WG, Stevenson LW. Prognostic significance of atrial fibrillation in advanced heart failure: A study of 390 patients. *Circulation* 1991;84:40-48.
2. **Middlekauff HR**, Stevenson WG, Tillisch JH. Sudden death prevention in myocardial infarction survivors: A decision analysis approach. *Am Heart J* 1992;123:475-480.
3. Stevenson WG, **Middlekauff HR**, Stevenson LW, Saxon LA, Woo MA, Moser D. Significance of aborted cardiac arrest and sustained ventricular tachycardia in patients referred for therapy of advanced heart failure. *Am Heart J* 1992;124:123-130.
4. **Middlekauff HR**, Wiener I, Saxon LA, Stevenson WG. Low dose amiodarone for atrial fibrillation: Time for a prospective study. *Ann Int Med* 1992;116:1017-1020.
5. **Middlekauff HR**, Stevenson WG, Stevenson LW, Saxon LA. Syncope in advanced heart failure: High sudden death risk regardless of syncope etiology. *J Am Coll Cardiol* 1993;21:110-116.
6. **Middlekauff HR**, Stevenson WG, Saxon LA. Prognosis following syncope: Impact of left ventricular function. *Am Heart J* 1993;125:121-127.
7. Saxon LA, Stevenson WG, **Middlekauff HR**, Fonarow G, Woo M, Moser D, Stevenson LW. Predicting death from progressive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. *Am J Cardiol* 1993;72:62-65.
8. Saxon LA, Stevenson WG, **Middlekauff HR**, Stevenson LW. Increased risk of progressive hemodynamic deterioration in adv. heart failure patients requiring permanent pacemakers. *Am Heart J* 1993;125:1306-10.
9. Stevenson WG, Khan H, Sager P, Saxon LA, **Middlekauff HR**, Natterson PD, Wiener I. Identification of reentry circuit sites during catheter mapping and radiofrequency ablation of ventricular tachycardia late after myocardial infarction. *Circulation* 1993;88:1647-1670.
10. Saxon LA, Stevenson WG, Fonarow GC, **Middlekauff HR**, Yeatman LA, Sherman CT, Child JS. Transesophageal echocardiography during radiofrequency catheter ablation of ventricular tachycardia. *Am J Cardiol* 1993;72:658-661.

11. Woo MA, Moser DK, **Middlekauff HR**, Stevenson WG. Relationship of serum norepinephrine and Poincaré plots in patients with advanced heart failure. *J Am Coll Cardiol* 1994;23:565-569.
12. **Middlekauff HR**, Hamilton MA, Stevenson LW, Mark AL. Independent control of skin and muscle sympathetic nerve activity in patients with heart failure. *Circulation* 1994;90:1794-1798.
13. Natterson PD, Stevenson WG, Saxon LA, **Middlekauff HR**, Stevenson LW. Risk of arterial embolization in 224 patients awaiting cardiac transplantation. *Am Heart J* 1995;129:564-70.
14. **Middlekauff HR**, Stevenson WG, Gornbein JA. Antiarrhythmic prophylaxis versus warfarin anticoagulation to prevent thromboembolic events among patients with atrial fibrillation: a decision analysis. *Arch Int Med* 1995;155:913-920.
15. **Middlekauff HR**, Sontz EM. Morning sympathetic nerve activity is not increased in humans: implications for mechanisms underlying the circadian pattern of cardiac risk. *Circulation* 1995;91:2549-2555.
16. Chun S, Sager PT, Stevenson WG, Nademanee K, **Middlekauff HR**, Singh BH. Refractory atrial fibrillation and flutter: clinical efficacy of amiodarone. *Am J Card* 1995;76:47-50.
17. **Middlekauff HR**, Nitzsche EU, Hamilton MA, Schelbert HR, Fonarow GC, Moriguchi JD, Hage A, Saleh S. Evidence for preserved cardiopulmonary baroreflex control of renal cortical blood flow in humans with advanced heart failure: a positron emission tomography study. *Circulation* 1995;92:395-401.
18. Stevenson WG, Sager P, Natterson PD, Saxon LA, **Middlekauff HR**, Wiener I. Relation of pace-mapping QRS morphology and conduction delay to ventricular tachycardia reentry circuits in human infarct scars. *J Am Coll Cardiol* 1995;26:481-8.
19. **Middlekauff HR**, Stevenson WG, Saxon LA, Stevenson LW. Amiodarone and torsades de pointes in patients with advanced heart failure. *Am J Cardiol* 1995;76:499-502.
20. Stevenson WG, Stevenson LW, **Middlekauff HR**, Fonarow GC, Hamilton MA, Woo MA, Saxon LA, Natterson PD, Steimle AE, Creaser J, Tillisch JH. Improving survival for patients with advanced heart failure: impact of clinical trials for 737 patients at a single center. *J Am Coll Cardiol* 1995;26:1417-1423.
21. Nguyen AH, Garfinkel A, Weiss JN, Walter DO, Hamilton MA, Fonarow GC, **Middlekauff HR**. Dynamics of sympathetic nerve activity in advanced heart failure patients. *Am J Physiol* 1996;271:H1962-H1969.
22. Stevenson WG, Stevenson LW, **Middlekauff HR**, Fonarow GC, Hamilton MA, Woo MA, Saxon LA, Natterson PD, Steimle A, Walden JA, Tillisch JH. Improving survival for patients with atrial fibrillation and advanced heart failure. *J Am Coll Cardiol* 1996;28:1458-63.
23. **Middlekauff HR**, Nitzsche EU, Nguyen AH, Hoh CK, Gibbs GG. Modulation of renal cortical blood flow during static exercise in humans. *Circ Res* 1997;80:62-68.
24. **Middlekauff HR**, Nguyen AH, Negrao CE, Nitzsche EU, Hoh CK, Natterson BA, Hamilton MA, Fonarow GC, Hage A, Moriguchi JD. Impact of acute mental stress on sympathetic nerve activity and regional blood flow in advanced heart failure: implications for "triggering" adverse cardiac events. *Circulation* 1997;96:1835-42.
25. **Middlekauff HR**, Rivkees SA, Raybould HE, Bitticaca M, Goldhaber JI, Weiss JN. Localization and functional effects of Adenosine (A₁) receptors on cardiac vagal afferent neurons in adult rats. *Am J Physiology* 1998;274:H441-H447.
26. Negrao CE, Hamilton MA, Fonarow GC, Hage A, Moriguchi JD, **Middlekauff HR**. Impaired endothelium - mediated vasodilation is not the principle cause of elevated vascular resistance in heart failure. *Am J Physiol* 2000;278:H168-H174.
27. **Middlekauff HR**, Nitzsche EU, Hoh CK, Hamilton MA, Fonarow GC, Hage A, Moriguchi JD. Exaggerated renal vasoconstriction during exercise in heart failure patients. *Circulation* 2000;101:784-789.
28. **Middlekauff HR**, Doering A, Weiss JN. Adenosine enhances neuroexcitability by inhibiting a slow post-spike after hyperpolarization in rabbit vagal afferent neurons. *Circulation* 2001;103:1325-29.
29. Negrao CE, Rondon MUPB, Tinucci T, Alves MJN, Roveda F, Braga AMW, Reis SF, Nastari L, Barretto ACP, Krieger EM, **Middlekauff HR**. Abnormal neurovascular control during exercise is linked to heart failure severity. *Am J Physiol Heart Circ Physiol* 2001;280:H1286-92.
30. **Middlekauff HR**, Yu JL, Hui, K. Acupuncture modulates reflex responses to mental stress in humans. *Am J Physiol Regul Integr Comp Physiol* 2001;280:R1462-68.
31. **Middlekauff HR**, Nitzsche EU, Hoh CK, Hamilton MA, Fonarow GC, Hage A, Moriguchi JD. Exaggerated muscle mechanoreflex control of reflex renal vasoconstriction in heart failure. *J Appl Physiol* 2001;90:1714-1719.
32. **Middlekauff HR**, Hui, KK, Yu JL, Hamilton MA, Fonarow GC, Moriguchi, J, MacLellan R, Hage A. Acupuncture inhibits sympathetic activation during mental stress in advanced heart failure patients. *J Cardiac Failure* 2002;8:399-406.

C. Research Support

Ongoing Research Support

5R01HL067298-02 Middlekauff (PI)

07/01/01 – 06/30/05

NIH/PHS

Muscle Mechanosensitivity in Heart Failure

Aim 1: To determine if ischemic metabolites acutely sensitize muscle mechanoreflex control of MSNA and RCVR, and whether this sensitization is exaggerated in HF. Reflex changes in MSNA and RCVR will be measured in HF patients and normal controls before and after administration of pharmacological agents to block ischemic metabolite activation during rhythmic handgrip, which selectively activates the muscle mechanoreceptors. Aim 2: To determine if muscle mechanoreceptors are chronically sensitized to contraction in patients with HF. Very mild rhythmic handgrip, involuntary contractions, and external arm compression will be performed in HF patients and normal controls to determine if mechanoreceptors are chronically sensitized in HF patients even in the absence of ischemic metabolites. Aim 3: To determine if exercise conditioning reverses exaggerated muscle mechanoreflex control in humans with HF. After a 4 week conditioning program, which reverses the myopathy of HF, the above testing repeated to determine if the muscle mechanoreceptor sensitization is reversible.

Role: PI

5R21AT000671-02 Middlekauff (PI)

7/15/01 – 06/30/03

NIH/NCCAM

Acupuncture in Cardiovascular Disease

The following hypotheses will be tested: 1) acupuncture, performed at traditional acupoints and non-acupoints in normal humans, stimulates skeletal muscle afferent neurons causing a release of endogenous opioids, which oppose sympathetic excitation and vasoconstriction in visceral vascular beds, such as the kidney; 2) in humans with HF in whom MSNA is elevated and renal vasoconstriction is the rule, acupuncture utilizes similar mechanisms as in normal humans to produce exaggerated inhibition of MSNA and reflex renal vasoconstriction. Positron emission tomography and I microneurography will be utilized to answer the following questions in normal humans and patients with heart failure: 1. Is acupuncture attenuation of BP during mental stress mediated by a decrease in renal vasoconstriction? 2. Is acupuncture sympathoinhibitory? 3. Is acupuncture modulation of the autonomic nervous system during mediated by muscle afferents? 4. Is acupuncture modulation of the autonomic nervous system mediated by activation of endogenous opioids? Understanding the mechanisms of acupuncture modulation of the autonomic nervous system in humans may help clarify its role as a therapeutic modality in cardiovascular diseases, such as heart failure.

Role: PI

Completed Research Support

N/A